```
=> dis his nofile l7-

     (FILE 'REGISTRY' ENTERED AT 18:10:48 ON 19 SEP 2007)
L7          454 SEA SSS FUL L4 OR L5

=> d l7 que stat
L4                STR
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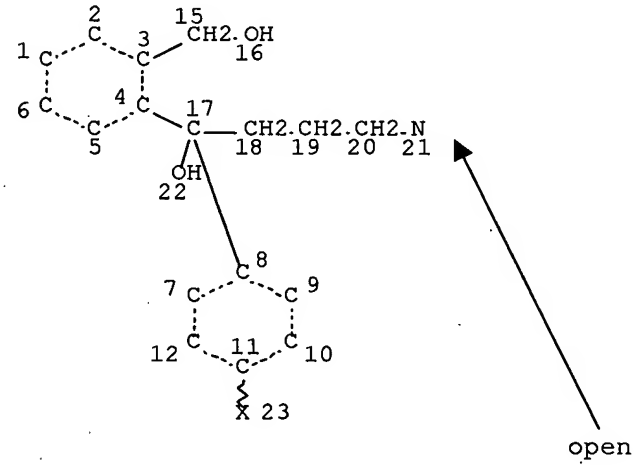


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  21

STEREO ATTRIBUTES: NONE
L5                STR
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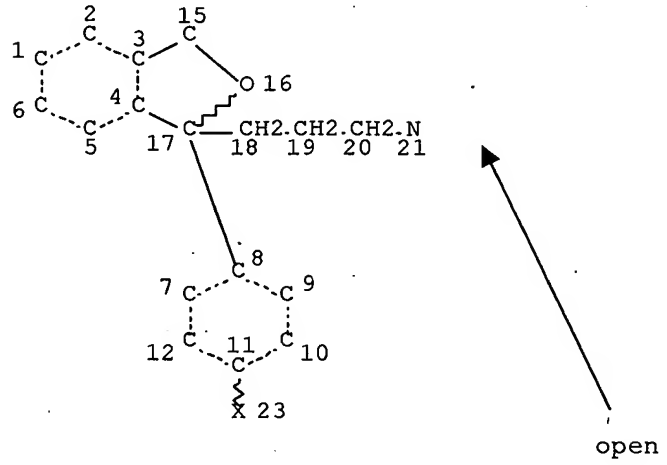


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
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NUMBER OF NODES IS  20

STEREO ATTRIBUTES: NONE
L7          454 SEA FILE=REGISTRY SSS FUL L4 OR L5

100.0% PROCESSED     615 ITERATIONS                          454 ANSWERS
SEARCH TIME: 00.00.01


=> fil medl,biosis,embase,caplus;s l7

FILE 'MEDLINE' ENTERED AT 18:15:00 ON 19 SEP 2007

FILE 'BIOSIS' ENTERED AT 18:15:00 ON 19 SEP 2007
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L8         1914 FILE MEDLINE
L9         2783 FILE BIOSIS
L10        9065 FILE EMBASE
L11        2372 FILE CAPLUS

TOTAL FOR ALL FILES
L12       16134 L7

=> s l12 and (method or prep?)
L13         679 FILE MEDLINE
L14        1181 FILE BIOSIS
L15        1786 FILE EMBASE
L16         923 FILE CAPLUS

TOTAL FOR ALL FILES
L17        4569 L12 AND (METHOD OR PREP?)

=> s crystall? or purif?
L18      868119 FILE MEDLINE
L19      462956 FILE BIOSIS
L20      316868 FILE EMBASE
L21     1768748 FILE CAPLUS

TOTAL FOR ALL FILES
L22     3416691 CRYSTALL? OR PURIF?

=> s l17 and l22
L23           8 FILE MEDLINE
L24          20 FILE BIOSIS
L25          12 FILE EMBASE
L26          62 FILE CAPLUS

TOTAL FOR ALL FILES
L27         102 L17 AND L22
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=> fil medl,biosis,embase;s l27

FILE 'MEDLINE' ENTERED AT 18:16:39 ON 19 SEP 2007

FILE 'BIOSIS' ENTERED AT 18:16:39 ON 19 SEP 2007
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L28             8 FILE MEDLINE
L29            20 FILE BIOSIS
L30            12 FILE EMBASE

TOTAL FOR ALL FILES
L31            40 L27

=> dup rem l31
PROCESSING COMPLETED FOR L31
L32            33 DUP REM L31 (7 DUPLICATES REMOVED)

=> d 1-33 ibib abs;fil caplus;s l27

L32  ANSWER 1 OF 33  EMBASE  COPYRIGHT (c) 2007 Elsevier B.V. All rights
     reserved on STN
ACCESSION NUMBER:    2007281024  EMBASE    Full-text
TITLE:               Irreversible binding of a novel phenylisothiocyanate
                     tropane analog to monoamine transporters in rat brain.
AUTHOR:              Murthy V.; Davies H.M.L.; Hedley S.J.; Childers S.R.
CORPORATE SOURCE:    S.R. Childers, Department of Physiology/Pharmacology,
                     Center for the Neurobiological Investigation of Drug Abuse,
                     Wake Forest University Health Sciences, Winston-Salem, NC
                     27157, United States. childers@wfubmc.edu
SOURCE:              Biochemical Pharmacology, (15 Jul 2007) Vol. 74, No. 2, pp.
                     336-344. .
                     Refs: 42
                     ISSN: 0006-2952  CODEN: BCPCA6
PUBLISHER IDENT.:    S 0006-2952(07)00259-6
COUNTRY:             United States
DOCUMENT TYPE:       Journal; Article
FILE SEGMENT:        029     Clinical Biochemistry
                     030     Pharmacology
                     037     Drug Literature Index
                     040     Drug Dependence, Alcohol Abuse and Alcoholism
                     008     Neurology and Neurosurgery
LANGUAGE:            English
SUMMARY LANGUAGE:    English
ENTRY DATE:          Entered STN: 28 Jun 2007
                     Last Updated on STN: 28 Jun 2007
AB   Irreversible tropane analogs have been useful in identifying binding sites of
     cocaine on biogenic amine transporters, including transporters for dopamine
     (DAT), serotonin (SERT) and norepinephrine (NET).  The present study
     characterizes the properties of the novel phenylisothiocyanate tropane HD-205,
     synthesized from the highly potent 2-napthyl tropane analog WF-23.  In
     radioligand binding studies in brain membranes, direct IC(50) values of HD-205
     were 4.1, 14 and 280 nM at DAT, SERT and NET, respectively.  Wash-resistant
     binding was characterized by preincubation of HD-205 with brain membranes,
     followed by extensive washing before performing transporter radioligand
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binding. Results for HD-205 showed wash-resistant IC(50) values of 191, 230 and 840 nM at DAT, SERT and NET, respectively. Saturation binding studies with [(125)I]RTI-55 in membranes pretreated with 100 nM HD-205 showed that HD-205 significantly decreased the B(max) but not K(D) of DAT and SERT binding. To further characterize its irreversible binding, an iodinated analog of HD-205, HD-244, was prepared from a trimethylsilyl precursor. The direct IC(50) of HD-244 at DAT was 20 nM. [(125)I]HD-244 was synthesized with chloramine-T, purified on HPLC, reacted with rat striatal membranes, and proteins were separated by SDS-PAGE. Results showed several non-specific labeled bands, but only a single specific band of radioactivity co-migrating with an immunoreactive DAT band at approx. 80 kilodaltons was detected, suggesting that [(125)I]HD-244 covalently labeled DAT protein in striatal membranes. These results demonstrate that phenylisothiocyanate analogs of WF-23 can be used as potential ligands to map distinct binding sites of cocaine analogs at DAT.

L32 ANSWER 2 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 1
ACCESSION NUMBER: 2006:349759 BIOSIS Full-text
DOCUMENT NUMBER: PREV200600342233
TITLE: Determination of antidepressants in surface and waste water samples by capillary electrophoresis with electrospray ionization mass spectrometric detection after preconcentration using off-line solid-phase extraction.
AUTHOR(S): Himmelsbach, Markus; Buchberger, Wolfgang; Klampfl, Christian W. [Reprint Author]
CORPORATE SOURCE: Johannes Kepler Univ, Inst Analyt Chem, Altenbergerstr 69, A-4040 Linz, Austria
christian.klampfl@jku.at
SOURCE: Electrophoresis, (MAR 2006) Vol. 27, No. 5-6, pp. 1220-1226.
CODEN: ELCTDN. ISSN: 0173-0835.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Jul 2006
Last Updated on STN: 12 Jul 2006

AB A method for the quantitative determination of seven major antidepressants in surface waters and sewage treatment plant effluents by CE using ESI-MS is presented. Calibration curves for the selected analytes were prepared in Milli-Q purified water and Danube river water extract covering a concentration range of at least one order of magnitude. LODs achieved were between 6 and 13 mu g/L for Trazodone and 39 and 53 mu g/L for Sertraline in the Milli-Q purified water and Danube river water matrix, respectively. For sample preparation eight different SPE materials were investigated. Best results were obtained for a resin based on hydrophilic divinylbenzene, (recoveries from Milli-Q purified water 93-96%; from Danube river water 85-99%). Finally, a series of eight sewage treatment plant effluents were investigated with respect to their content in the selected antidepressants. Six of these samples were tested positive for antidepressants, in particular Venlafaxine, Citalopram and Trazodone in concentrations between 36 and 322 ng/L.

L32 ANSWER 3 OF 33 EMBASE
ACCESSION NUMBER: 2006211751 EMBASE Full-text
TITLE: HPLC analysis of the second-generation antidepressant sertraline and its main metabolite N-desmethylsertraline in human plasma.
AUTHOR: Mandrioli R.; Saracino M.A.; Ferrari S.; Berardi D.;

Kenndler E.; Raggi M.A.
CORPORATE SOURCE: M.A. Raggi, Faculty of Pharmacy, Department of Pharmaceutical Sciences, Alma Mater Studiorum - University of Bologna, Via Belmeloro 6, I-40126 Bologna, Italy. mariaaugusta.raggi@unibo.it
SOURCE: Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences, (19 May 2006) Vol. 836, No. 1-2, pp. 116-119. .
Refs: 18.
ISSN: 1570-0232 CODEN: JCBAAI
PUBLISHER IDENT.: S 1570-0232(06)00246-7
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 8 Jun 2006
Last Updated on STN: 8 Jun 2006

AB A liquid chromatographic method with ultraviolet detection was developed for the analysis of the recent antidepressant sertraline and its main metabolite N-desmethylsertraline in human plasma. The analytes were separated on a C8 reversed phase column, using a mobile phase composed of acetonitrile and a 12.3 mM, pH 3.0 phosphate buffer containing 0.1% triethylamine (35:65, v/v). Clomipramine was used as the Internal Standard. Using a solid phase extraction procedure with C2 cartridges high extraction yields (>94%) and good purification from matrix interference were obtained. Good linearity was obtained in the 7.5-250.0 ng mL(-1) range for sertraline and in the 10-500 ng mL(-1) range for N-desmethylsertraline. The analytical method was validated in terms of precision, extraction yield and accuracy. These assays gave R.S.D.% values for precision always lower than 3.9% and mean accuracy higher than 90%. Thanks to its good selectivity, the method proved to be suitable for the analysis of plasma samples from patients treated with sertraline as either monotherapy or polypharmacy. .COPYRGT. 2006 Elsevier B.V. All rights reserved.

L32 ANSWER 4 OF 33 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006411357 EMBASE Full-text
TITLE: AClAP, Autonomous hierarchical agglomerative Cluster Analysis based protocol to partition conformational datasets.
AUTHOR: Bottegoni G.; Rocchia W.; Recanatini M.; Cavalli A.
CORPORATE SOURCE: A. Cavalli, Department of Pharmaceutical Sciences, University of Bologna, Via Belmeloro 6, I-40126 Bologna, Italy. andrea.cavalli@unibo.it
SOURCE: Bioinformatics, (15 Jul 2006) Vol. 22, No. 14, pp. e58-e65. .
Refs: 18
ISSN: 1367-4803 E-ISSN: 1460-2059 CODEN: BOINFP
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 15 Sep 2006
Last Updated on STN: 15 Sep 2006

AB Motivation: Sampling the conformational space is a fundamental step for both ligand- and structure-based drug design. However, the rational organization of different molecular conformations still remains a challenge. In fact, for drug design applications, the sampling process provides a redundant conformation set whose thorough analysis can be intensive, or even prohibitive. We propose a statistical approach based on cluster analysis aimed at rationalizing the output of methods such as Monte Carlo, genetic, and reconstruction algorithms. Although some software already implements clustering procedures, at present, a universally accepted protocol is still missing. Results: We integrated hierarchical agglomerative cluster analysis with a clusterability assessment method and a user independent cutting rule, to form a global protocol that we implemented in a MATLAB metalanguage program (AClAP). We tested it on the conformational space of a quite diverse set of drugs generated via Metropolis Monte Carlo simulation, and on the poses we obtained by reiterated docking runs performed by four widespread programs. In our tests, AClAP proved to remarkably reduce the dimensionality of the original datasets at a negligible computational cost. Moreover, when applied to the outcomes of many docking programs together, it was able to point to the crystallographic pose.

L32 ANSWER 5 OF 33 MEDLINE on STN
ACCESSION NUMBER: 2005145814 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15706576
TITLE: Analysis of serotonin in brain microdialysates using capillary electrophoresis and native laser-induced fluorescence detection.
AUTHOR: Benturquia Nadia; Couderc Francois; Sauvinet Valerie; Orset Cyrille; Parrot Sandrine; Bayle Christophe; Renaud Bernard; Denoroy Luc
CORPORATE SOURCE: Laboratoire de Neuropharmacologie et Neurochimie, INSERM U512, Institut Federatif des Neurosciences de Lyon (IFR 19), Universite Claude Bernard, F-69373 Lyon Cedex 08, France.
SOURCE: Electrophoresis, (2005 Mar) Vol. 26, No. 6, pp. 1071-9. Journal code: 8204476. ISSN: 0173-0835.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (VALIDATION STUDIES)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200508
ENTRY DATE: Entered STN: 22 Mar 2005
Last Updated on STN: 6 Aug 2005
Entered Medline: 5 Aug 2005

AB Serotonin or 5-hydroxytryptamine (5-HT) is a major neurotransmitter in the central nervous system. In this work, a method for analyzing 5-HT in brain microdialysis samples using a commercially available capillary electrophoresis (CE) system has been developed. A pH-mediated in-capillary preconcentration of samples was performed, and after separation by capillary zone electrophoresis, native fluorescence of 5-HT was detected by a 266 nm solid-state laser. The separation conditions for the analysis of 5-HT in standard solutions and microdialysates have been optimized, and this method has been validated on both pharmacological and analytical bases. Separation of 5-HT was performed using a 80 mmol/L citrate buffer, pH 2.5, containing 20 mmol/L hydroxypropyl-beta-cyclodextrin (HP-beta-CD) and +30 kV voltage. The detection limit was 2.5 x 10(-10) mol/L. This method allows the in vivo brain monitoring of 5-HT using a simple, accurate CE measurement in underivatized microdialysis samples.

L32 ANSWER 6 OF 33 MEDLINE on STN
ACCESSION NUMBER: 2005248169 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15814274
TITLE: Alkaloids from Boophane disticha with affinity to the serotonin transporter in rat brain.
AUTHOR: Sandager Mikkel; Nielsen Nicolaj D; Stafford Gary I; van Staden Johannes; Jager Anna K
CORPORATE SOURCE: Research Centre for Plant Growth and Development, School of Botany and Zoology, University of KwaNatal Pietermaritzburg, P/Bag X01, Scottsville 3209, South Africa.
SOURCE: Journal of ethnopharmacology, (2005 Apr 26) Vol. 98, No. 3, pp. 367-70.
Journal code: 7903310. ISSN: 0378-8741.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 13 May 2005
Last Updated on STN: 21 Jul 2005
Entered Medline: 20 Jul 2005

AB Bulbs and leaves of Boophane disticha are used in South African traditional medicine in the treatment of anxiety. Crude extracts of the leaves have shown affinity to the SSRI site on the serotonin transporter in a radioligand binding assay. In this study, two compounds, buphanadrine and buphanamine, were isolated by bioassay-guided fractionation on VLC and preparative TLC. The structures of the compounds were determined by (1)H and (13)C NMR. Fractions were tested for affinity to the serotonin transporter in a binding assay using [(3)H]-citalopram as ligand. The IC(50) values of buphanidrine and buphanamine were 274 microM (K(i)=132 microM) and 1799 microM (K(i)=868 microM), respectively. The two alkaloids were also tested for affinity to the 5HT(1A) receptor, but only showed slight affinity.

L32 ANSWER 7 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:383183 BIOSIS Full-text
DOCUMENT NUMBER: PREV200400388202
TITLE: Preparation of pure citalopram.
AUTHOR(S): Kaushik, Vipin Kumar [Inventor, Reprint Author]; Rao, Divvela Venkata Naga Srinivasa [Inventor]; Handa, Vijay Kumar [Inventor]; Sivakumaran, Meenakshisunderam [Inventor]
CORPORATE SOURCE: Hyderabad, India
ASSIGNEE: Aurobindo Pharma Ltd., Hyderabad, India
PATENT INFORMATION: US 6781003 20040824
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Aug 24 2004) Vol. 1285, No. 4.
http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Sep 2004
Last Updated on STN: 29 Sep 2004

AB The present invention relates to an industrially advantageous method for the purification of Citalopram (Formula I) wherein desmethyl citalopram (Formula II), present in crude Citalopram as an impurity, is methylated to produce pure

Citalopram. The resulting Citalopram product is isolated as the base or a pharmaceutically acceptable salt thereof ##STR1##

L32 ANSWER 8 OF 33 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004443263 EMBASE Full-text
TITLE: A rapid HPLC-DAD method for the analysis of fluoxetine and norfluoxetine in plasma from overdose patients.
AUTHOR: Sabbioni C.; Bugamelli F.; Varani G.; Mercolini L.; Musenga A.; Saracino M.A.; Fanali S.; Raggi M.A.
CORPORATE SOURCE: M.A. Raggi, Dept. of Pharmaceutical Sciences, Faculty of Pharmacy, Alma Mater Studiorum - Univ. B., Bologna, Italy. mariaaugusta.raggi@unibo.it
SOURCE: Journal of Pharmaceutical and Biomedical Analysis, (29 Oct 2004) Vol. 36, No. 2, pp. 351-356. .
Refs: 41
ISSN: 0731-7085 CODEN: JPBADA
PUBLISHER IDENT.: S 0731-7085(04)00262-6
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
039 Pharmacy
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Nov 2004
Last Updated on STN: 12 Nov 2004

AB There is a need for fast, simple and reliable analytical methods for the analysis of fluoxetine and norfluoxetine in patients who voluntarily or involuntarily have taken an overdose of the drug. A new liquid chromatographic method with diode array detection is presented herein for the determination of fluoxetine and its main active metabolite in human plasma for toxicological purposes. A mobile phase composed of acetonitrile and aqueous tetramethylammonium perchlorate allows to obtain the complete separation of the analytes on a C18 reversed phase column. The fast and accurate sample pre-treatment step is carried out by means of solid-phase extraction using hydrophilic-lipophilic balance cartridges and loading 100 μL of plasma only. This procedure gives satisfactory extraction yield values, as well as good plasma sample purification from matrix interference. Linearity was obtained in the 150-3000 ng/mL range for both analytes. Selectivity with respect to other psychotropic drugs was satisfactory. The method seems to be suitable for the analysis of fluoxetine and its metabolite in human plasma for depressed patients in overdose.

L32 ANSWER 9 OF 33 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2004209814 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15107147
TITLE: A comparative solid-phase extraction study for the simultaneous determination of fluvoxamine, mianserin, doxepin, citalopram, paroxetine, and etoperidone in whole blood by capillary gas-liquid chromatography with nitrogen-phosphorus detection.
AUTHOR: Martinez Maria A; Sanchez de la Torre Carolina; Almarza Elena
CORPORATE SOURCE: Department of Chemistry, National Institute of Toxicology, Ministry of Justice. C/Luis Cabrera 9, 28002 Madrid,

Spain.. mariantmart@terra.es
SOURCE: Journal of analytical toxicology, (2004 Apr) Vol. 28, No. 3, pp. 174-80.
Journal code: 7705085. ISSN: 0146-4760.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
(COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 27 Apr 2004
Last Updated on STN: 11 Nov 2004
Entered Medline: 10 Nov 2004

AB This paper reports a simple and reliable gas chromatographic method with nitrogen-phosphorus detection without derivatization for the simultaneous detection of fluvoxamine, mianserin, doxepin, citalopram, paroxetine, and etoperidone in whole blood as part of a systematic toxicological analysis (STA). All drugs were studied at concentration levels of 100-2000 ng/mL, except paroxetine for which it was necessary to study at concentration levels of 400-8000 ng/mL. A comparative and validation study using two solid-phase extraction (SPE) columns, Chem Elut and Bond Elut Certify, was developed regarding their recovery, precision, sensitivity, and matrix purification efficiency. The Chem Elut columns, diatomaceous earth, are closely related to conventional liquid-liquid extraction. The Bond Elut Certify columns, more recently developed in the market, are mixed SPE (reversed-phase and cation exchange sorbent). Recoveries for the antidepressants using Chem Elut columns at 500 ng/mL (2000 ng/mL for paroxetine) were in the range 43-72% with intra- and interassay precisions of less than 10% and 16%, respectively. Limits of detection (LODs) and quantitation (LOQs) for fluvoxamine, mianserin, doxepin, citalopram, and etoperidone ranged from 18 to 236 ng/mL and 60 to 786 ng/mL, respectively. LOD and LOQ for paroxetine were 303 and 1009 ng/mL, respectively. Recoveries of these compounds using Bond Elut Certify columns at 500 ng/mL (2000 ng/mL for paroxetine) were in the range 52-83% with intra- and interassay precisions of less than 6% and 8%, respectively. LODs and LOQs for fluvoxamine, mianserin, doxepin, citalopram, and etoperidone ranged from 7 to 28 ng/mL and 23 to 93 ng/mL, respectively. LOD and LOQ for paroxetine were 113 and 376 ng/mL, respectively. An excellent linearity was observed with both procedures from the LOQs up to the upper studied concentration level. In general, higher recoveries, cleaner extracts, better sensitivity, better precision, and reduced solvent consumption and disposal were achieved for the screening of these antidepressants with the use of the mixed SPE Bond Elut Certify compared with Chem Elut columns. The application of these methods on a forensic case study is also presented.

L32 ANSWER 10 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:487116 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300488806
TITLE: Carbonic anhydrase activators. The selective serotonin reuptake inhibitors fluoxetine, sertraline and citalopram are strong activators of isozymes I and II.
AUTHOR(S): Casini, Angela; Caccia, Silvio; Scozzafava, Andrea; Supuran, Claudiu T. [Reprint Author]
CORPORATE SOURCE: Dipartimento di Chimica, Laboratorio di Chimica Bioinorganica, Universita degli Studi di Firenze, Via della Lastruccia 3, Rm. 188, I-50019, Sesto Fiorentino, Firenze, Italy
claudiu.supuran@unifi.it

SOURCE: Bioorganic & Medicinal Chemistry Letters, (18 August 2003) Vol. 13, No. 16, pp. 2765-2768. print.
CODEN: BMCLE8. ISSN: 0960-894X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Oct 2003
Last Updated on STN: 22 Oct 2003

AB The selective serotonin reuptake inhibitors (SSRI) fluoxetine, sertraline and citalopram have been investigated for their ability to activate two carbonic anhydrase (CA) isozymes, hCA I and hCA II, in parallel with two standard activators for which the X-ray structure (in complex with isozyme II) has been resolved: histamine and phenylalanine. All three SSRI activated both isozymes with potencies comparable to that of the standards although the profile was different: for hCA I, best activators were fluoxetine and histamine, with citalopram and sertraline showing weaker activity. For hCA II, the best activators were phenylalanine and citalopram, and the weakest histamine and sertraline, whereas fluoxetine showed an intermediate behavior. These results suggest that SSRI efficacy in major depression complicating Alzheimer's disease may be partly due to their ability to activate CA isozymes and may lead to the development of potent activators for the therapy of diseases associated with significant decreases in brain CA activity.

L32 ANSWER 11 OF 33 MEDLINE on STN

ACCESSION NUMBER: 2003366140 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12900873
TITLE: Enantiomeric separation of citalopram and its metabolites by capillary electrophoresis.
AUTHOR: Mandrioli Roberto; Fanali Salvatore; Pucci Vincenzo; Raggi Maria A
CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Bologna, Via Belmeloro 6, I-40126 Bologna, Italy.
SOURCE: Electrophoresis, (2003 Aug) Vol. 24, No. 15, pp. 2608-16.
Journal code: 8204476. ISSN: 0173-0835.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 6 Aug 2003
Last Updated on STN: 18 Jun 2004
Entered Medline: 17 Jun 2004

AB A simple and fast capillary electrophoretic method has been developed for the enantioselective separation of citalopram and its main metabolites, namely N-desmethylcitalopram and N,N-didesmethylcitalopram, using beta-cyclodextrin (beta-CD) sulfate as the chiral selector. For method optimisation several parameters were investigated, such as CD and buffer concentration, buffer pH, and capillary temperature. Baseline enantioseparation of the racemic compounds was achieved in less than 6 min using a fused-silica capillary, filled with a background electrolyte consisting of a 35 mM phosphate buffer at pH 2.5 supplemented with 1% w/v beta-CD sulfate and 0.05% w/v beta-CD at 25 degrees C and applying a voltage of -20 kV. A fast separation method for citalopram was also optimized and applied to the analysis of pharmaceutical formulations. Racemic citalopram was resolved in its enantiomers in less than 1.5 min using short-end injection (8.5 cm, effective length) running the experiments in a background electrolyte composed of a 25 mM citrate buffer at pH 5.5 and 0.04% w/v beta-CD sulfate at a temperature of 10 degrees C.

L32 ANSWER 12 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on

STN
ACCESSION NUMBER: 2002:234649 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200234649
TITLE: A reversed-phase HPLC method development for the separation of new antidepressants.
AUTHOR(S): Dallet, P. [Reprint author]; Labat, L.; Richard, M.; Langlois, M. H.; Dubost, J. P.
CORPORATE SOURCE: Laboratoire de Chimie Analytique, UFR Pharmacie, Universite Victor Segalen, 3 ter Place de la Victoire, F-33076, Bordeaux Cedex, France
philippe.dallet@u-bordeaux2.fr
SOURCE: Journal of Liquid Chromatography and Related Technologies, (January, 2002) Vol. 25, No. 1, pp. 101-111. print.
ISSN: 1082-6076.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Apr 2002
Last Updated on STN: 10 Apr 2002

AB A RPLC method with UV detection (225 nm) is developed for the separation of five SSRIs (fluvoxamine, fluoxetine, sertraline, paroxetine, and citalopram), two SNaRIS (venlafaxine and milnacipran), one NaSSA (mirtazapine), and four active metabolites (norfluoxetine, desmethylcitalopram, desmethylvenlafaxine, and desmethylmirtazapine). A standard solution (20 mug/mL) of the twelve compounds is analysed under isocratic conditions on two new-generation RP columns (Satisfaction(R) RP 18 AB and Satisfaction(R) C8+, 250 mmX4.6 mm, 5 mum). Mobile phase composition (acetonitrile content, pH of the aqueous buffer) and temperature are varied and the effect of these parameters on the retention factors of the antidepressants is examined. Similar elution profiles are observed with the two stationary phases, but the separation of all the solutes is only possible on the RP 18 AB column. It can be achieved at 45degreeC (or 50degreeC) with a mobile phase consisting of a mixture of potassium dihydrogen phosphate (pH 4.8, 25 mM)-acetonitrile (65:35, v/v) (flow rate: 1 mL/min). The run time is 20 min and a baseline resolution is obtained for all the analytes allowing this procedure to be well suited for a rapid toxicological screening.

L32 ANSWER 13 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:300886 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200300886
TITLE: Simultaneous determination of citalopram, fluoxetine, paroxetine and their metabolites in plasma by temperature-programmed packed capillary liquid chromatography with on-column focusing of large injection volumes.
AUTHOR(S): Molander, P. [Reprint author]; Thomassen, A.; Kristoffersen, L.; Greibrokk, T.; Lundanes, E.
CORPORATE SOURCE: National Institute of Occupational Health, N-0033, Oslo, Norway
pal.molander@stami.no
SOURCE: Journal of Chromatography B, (5 January, 2002) Vol. 766, No. 1, pp. 77-87. print.
ISSN: 1387-2273.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 May 2002
Last Updated on STN: 25 Jun 2002

AB A miniaturized temperature-programmed packed capillary liquid chromatographic method with on-column large volume injection and UV detection for the

simultaneous determination of the three selective serotonin reuptake inhibitors citalopram, fluoxetine, paroxetine and their metabolites in plasma is presented. An established reversed-phase C8 solid-phase extraction method was employed, and the separation was carried out on a 3.5-mum Kromasil C18 0.32X300 mm column with temperature-programming from 35 (3 min) to 100degreeC (10 min) at 1.3degreeC/min. The mobile phase consisted of acetonitrile-45 mM ammonium formate (pH 4.00) (25:75, v/v). The non-eluting sample focusing solvent composition acetonitrile-45 mM ammonium formate (pH 4.00) (3:97, v/v) allowed injection of 10 mul or more of the plasma extracts. The method was validated for the concentration range 0.05-5.0 muM, and the calibration curves were linear with coefficients of correlation >0.993. The limits of quantification for the antidepressants and their metabolites ranged from 0.05 to 0.26 muM. The within and between assay precision of relative peak height were in the range 2-22 and 2-15% relative standard deviation, respectively. The within and between assay recoveries were in the 61-99 and 54-92% range for the antidepressants, respectively, and between 52-102 and 51-102% for the metabolites.

L32 ANSWER 14 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:380597 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200380597
TITLE: Separation of new antidepressants and their metabolites by micellar electrokinetic capillary chromatography.
AUTHOR(S): Labat, L.; Deveaux, M. [Reprint author]; Dallet, P.; Dubost, J. P.
CORPORATE SOURCE: Institut de Medecine Legale, Place Theo Varlet, 59000, Lille, France
mdeveaux@easynet.fr
SOURCE: Journal of Chromatography B, (15 June, 2002) Vol. 773, No. 1, pp. 17-23. print.
ISSN: 1387-2273.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Jul 2002
Last Updated on STN: 10 Jul 2002

AB Selective serotonin reuptake inhibitors (SSRIs), serotonin noradrenergic reuptake inhibitors (SNaRIs) and noradrenergic and specific serotoninergic antidepressant (NaSSA) are widely used in the treatment of depression. An increase in antidepressant intoxications led to the development of reliable analytical methods for their analysis. A new determination procedure for these compounds (milnacipran, venlafaxine, desmethylvenlafaxine, mirtazapine, desmethylmirtazapine, citalopram, desmethylcitalopram, fluvoxamine, paroxetine, sertraline and fluoxetine) was developed by micellar electrokinetic capillary chromatography (MEKC) with diode array detection (DAD). Separation and determination were optimised on an uncoated fused-silica capillary (600 mm, 75 mum I.D.). The migration buffer consisted of 20 mM sodium borate, pH 8.55, with 20 mM SDS and 15% isopropanol, at an operating voltage of 25 kV. The column temperature was maintained at 40degreeC. Injection in the capillary was performed in the hydrodynamic mode (0.5 p.s.i., 15 s). In these conditions, the migration time of the antidepressants was less than 11 min. In most cases, calibration curves were established for 30-2000 ng/ml (r>0.995). The limit of detection and the limit of quantification were ranged between 10 and 20 and between 20 and 30 ng/ml, respectively, for all the molecules. This method allowed the determination of some of these compounds in biological fluids (blood, urine) in post-mortem cases. Samples (1 ml) were extracted with diethyl ether (5 ml) at pH 9.6 and reconstituted in diluted migration buffer. Similar results were obtained by a HPLC-DAD determination, performed as a reference method. These results suggest that

this MEKC method can be useful for the determination of new antidepressants in post-mortem cases.

L32 ANSWER 15 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:364674 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100364674
TITLE: Biophysical characterization of the cocaine binding pocket in the serotonin transporter using a fluorescent cocaine analogue as a molecular reporter.
AUTHOR(S): Rasmussen, Soren G. F.; Carroll, F. Ivy; Maresch, Martin J.; Jensen, Anne Dam; Tate, Christopher G.; Gether, Ulrik [Reprint author]
CORPORATE SOURCE: Div. of Cellular and Molecular Physiology, Dept. of Medical Physiology 12-5-22, Panum Institute, University of Copenhagen, DK-2200, Copenhagen N, Denmark gether@mfi.ku.dk
SOURCE: Journal of Biological Chemistry, (February 16, 2001) Vol. 276, No. 7, pp. 4717-4723. print. CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Aug 2001
Last Updated on STN: 23 Feb 2002

AB To explore the biophysical properties of the binding site for cocaine and related compounds in the serotonin transporter SERT, a high affinity cocaine analogue (3beta-(4-methylphenyl)tropane-2beta-carboxylic acid N-(N-methyl-N-(4-nitrobenzo-2-oxa-1,3-diazol-7-yl)ethanolamine ester hydrochloride (RTI-233; KI = 14 nM) that contained the environmentally sensitive fluorescent moiety 7-nitrobenzo-2-oxa-1,3-diazole (NBD) was synthesized. Specific binding of RTI-233 to the rat serotonin transporter, purified from Sf-9 insect cells, was demonstrated by the competitive inhibition of fluorescence using excess serotonin, citalopram, or RTI-55 (2beta-carbomethoxy-3beta-(4-iodophenyl)tropane). Moreover, specific binding was evidenced by measurement of steady-state fluorescence anisotropy, showing constrained mobility of bound RTI-233 relative to RTI-233 free in solution. The fluorescence of bound RTI-233 displayed an emission maximum (lambdamax) of 532 nm, corresponding to a 4-nm blue shift as compared with the lambdamax of RTI-233 in aqueous solution and corresponding to the lambdamax of RTI-233 in 80% dioxane. Collisional quenching experiments revealed that the aqueous quencher potassium iodide was able to quench the fluorescence of RTI-233 in the binding pocket (KSV = 1.7 M-1), although not to the same extent as free RTI-233 (KSV = 7.2 M-1). Conversely, the hydrophobic quencher 2,2,6,6-tetramethylpiperidine-N-oxyl (TEMPO) quenched the fluorescence of bound RTI-233 more efficiently than free RTI-233. These data are consistent with a highly hydrophobic microenvironment in the binding pocket for cocaine-like uptake inhibitors. However, in contrast to what has been observed for small-molecule binding sites in, for example, G protein-coupled receptors, the bound cocaine analogue was still accessible for aqueous quenching and, thus, partially exposed to solvent.

L32 ANSWER 16 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:216204 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100216204
TITLE: On-line extraction using an alkyl-diol silica precolumn for racemic citalopram and its metabolites in plasma: Results compared with solid-phase extraction methodology.
AUTHOR(S): Ohman, Daniel [Reprint author]; Carlsson, Bjorn; Norlander,

Bjorn
CORPORATE SOURCE: Department of Medicine and Care, Clinical Pharmacology, Faculty of Health Sciences, Linkoping University, S-581 85, Linkoping, Sweden
SOURCE: Journal of Chromatography B, (5 April, 2001) Vol. 753, No. 2, pp. 365-373. print.
CODEN: JCBADL. ISSN: 0378-4347.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 2 May 2001
Last Updated on STN: 18 Feb 2002

AB Sample preparation is usually the most critical and time consuming step when using HPLC for drug analysis in biological matrixes. Sample extracts have to be clean considering both chromatographic interferences and column maintenance. To meet some of these criteria a fully automated on-line extraction (OLE) analysis method was developed for the antidepressant drug citalopram and its two demethylated metabolites, using an RP-C4-ADS extraction column. A comparison between the new OLE method and an off-line solid-phase extraction method showed that the two methodologies were equal in analytical precision but that the OLE method was faster and therefore superior in sample capacity per day.

L32 ANSWER 17 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:434048 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100434048
TITLE: Reduction of extraction times in liquid-phase microextraction.
AUTHOR(S): Halvorsen, Trine Gronhaug [Reprint author]; Pedersen-Bjergaard, Stig; Rasmussen, Knut E.
CORPORATE SOURCE: School of Pharmacy, University of Oslo, Blindern, 0316, Oslo, Norway
t.g.halvorsen@farmasi.uio.no
SOURCE: Journal of Chromatography B, (5 September, 2001) Vol. 760, No. 2, pp. 219-226. print.
CODEN: JCBADL. ISSN: 0378-4347.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Sep 2001
Last Updated on STN: 22 Feb 2002

AB Recently, we introduced a simple and inexpensive disposable device for liquid-phase microextraction (LPME) based on porous polypropylene hollow fibres. In the present paper, extraction times were significantly reduced by an increase in the surface of the hollow fibres. The model compounds methamphetamine and citalopram, were extracted from 2.5 ml of urine, plasma, and whole blood after dilution with water and alkalisation with 125 mul of 2 M NaOH though a porous polypropylene hollow fibre impregnated with hexyl ether and into an aqueous acceptor phase consisting of 0.1 M HCl. Two commercially available hollow fibres, which differed in surface area, wall thickness and internal diameter, were compared. An increase in the contact area of the hollow fibre with the sample solution by a factor of approximately two resulted in reduction in equilibrium times by approximately the same factor. Thus, the model compounds were extracted to equilibrium within 15 min from both urine and plasma, and within 30 min from whole blood. For the first time LPME was utilised to extract drugs from whole blood, and the extracts were comparable with plasma both with regard to sample clean-up and extraction recoveries. Extraction recoveries for methamphetamine and citalopram varied from 60 to 100% using the two fibres and the different matrices.

L32 ANSWER 18 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:496998 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100496998
TITLE: High-performance liquid chromatographic method to screen and quantitate seven selective serotonin reuptake inhibitors in human serum.
AUTHOR(S): Tournel, G. [Reprint author]; Houdret, N.; Hedouin, V.; Deveaux, M.; Gosset, D.; Lhermitte, M.
CORPORATE SOURCE: Faculte de Medecine, Institut de Medecine Legale de Lille, Universite de Lille II, Place Theo Varlet, 59000, Lille, France
SOURCE: Journal of Chromatography B, (25 September, 2001) Vol. 761, No. 2, pp. 147-158. print.
CODEN: JCBADL. ISSN: 0378-4347.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Oct 2001
Last Updated on STN: 23 Feb 2002

AB A high-performance liquid chromatographic screening method (HPLC) is described for the determination of seven selective serotonin reuptake inhibitors (SSRIs) (fluvoxamine, milnacipran, paroxetine, sertraline, fluoxetine, citalopram, venlafaxine) and for three pharmacologically active N-demethylated metabolites (desmethylcitalopram, didesmethylcitalopram and norfluoxetine). A tricyclic antidepressant, clomipramine, was used as an internal standard. The method consists of liquid extraction of serum after alcalinisation at pH 9.50, followed by chromatography on a Beckman C18 reversed-phase column. Compounds were detected at 200.4 nm. The standard curves were linear over a working range of 50-1000 ng/ml for fluvoxamine, 15-1000 ng/ml for fluoxetine, 25-500 ng/ml for norfluoxetine, 50-500 ng/ml for sertraline, 20-500 ng/ml for paroxetine, 25-550 ng/ml for citalopram, 25-750 ng/ml for desmethylcitalopram, 25-800 ng/ml for didesmethylcitalopram, 25-650 ng/ml for milnacipran, and 25-500 ng/ml for venlafaxine. The quantitation limits of the method were 15 ng/ml for fluoxetine, 20 ng/ml for paroxetine, 25 ng/ml for venlafaxine, norfluoxetine and citalopram, and its metabolites, 40 ng/ml for sertraline and 50 ng/ml for fluvoxamine. No interferences were noted with this sensitive and specific method which can be used for therapeutic drug monitoring.

L32 ANSWER 19 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:110815 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100110815
TITLE: Liquid-phase microextraction and capillary electrophoresis of citalopram, an antidepressant drug.
AUTHOR(S): Halvorsen, Trine Gronhaug [Reprint author]; Pedersen-Bjergaard, Stig; Rasmussen, Knut E.
CORPORATE SOURCE: School of Pharmacy, University of Oslo, 0316, Oslo, Norway t.g.halvorsen@farmasi.uio.no
SOURCE: Journal of Chromatography A, (9 February, 2001) Vol. 909, No. 1, pp. 87-93. print.
CODEN: JOCRAM. ISSN: 0021-9673.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Feb 2001
Last Updated on STN: 15 Feb 2002

AB A newly developed disposable device for liquid-phase microextraction (LPME) was evaluated for the capillary electrophoresis (CE) of the antidepressant drug citalopram (CIT) and its main metabolite N-desmethylcitalopram (DCIT) in

human plasma. CIT and DCIT were extracted from 1 ml plasma samples through hexyl ether immobilised in the pores of a porous polypropylene hollow fibre and into 25 mul of 20 mM phosphate buffer (pH 2.75) present inside the hollow fibre (acceptor phase). Prior to extraction, the samples were made strongly alkaline in order to promote LPME of the basic drugs. Owing to the high ratio between the volumes of sample and acceptor phase, and owing to high partition coefficients, CIT and DCIT were enriched by a factor of 25 to 30. In addition, sample clean-up occurred during LPME since salts, proteins and the majority of endogenic substances were unable to penetrate the hexyl ether layer. Since the extracts were aqueous, they were injected directly into the CE instrument. Limits of quantification (S/N=10) for CIT and DCIT in plasma were 16.5 ng/ml and 18 ng/ml respectively, while the limits of detection (S/N=3) were 5 ng/ml and 5.5 ng/ml respectively. This enabled CIT (and DCIT) to be analysed within the therapeutic range by LPME-CE and detection limits were comparable with previously reported HPLC methods.

L32 ANSWER 20 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:352780 BIOSIS Full-text
DOCUMENT NUMBER: PREV200000352780
TITLE: Methods for the determination of seven selective serotonin reuptake inhibitors and three active metabolites in human serum using high-performance liquid chromatography and gas chromatography.
AUTHOR(S): Lacassie, E. [Reprint author]; Gaulier, J.-M.; Marquet, P.; Rabatel, J.-F.; Lachatre, G.
CORPORATE SOURCE: Department of Pharmacology and Toxicology, University Hospital, 2 Av. Martin Luther King, 87042, Limoges, France
SOURCE: Journal of Chromatography B, (9 June, 2000) Vol. 742, No. 2, pp. 229-238. print.
CODEN: JCBADL. ISSN: 0378-4347.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Aug 2000
Last Updated on STN: 8 Jan 2002

AB This paper describes a set of simple and sensitive multiresidue methods for the determination of the specific serotonin reuptake inhibitors (SSRIs) used as antidepressant drugs, and some of their respective active metabolites in human serum. It involves liquid-liquid extraction procedures followed by gas chromatography coupled to nitrogen phosphorus detection or isocratic reversed-phase high-performance liquid chromatography combined with fluorescence detection (HPLC-FL), depending on the analytes. Extraction recoveries were between 71 and 96% for the eight SSRIs and their metabolites analysed by GC and between 41 and 77% for the two of them analysed by HPLC. Limits of detection (LODs) and limits of quantitation (LOQs) ranged, respectively, from 2.5 to 5 mug/l and from 10 to 20 mug/l. Intra-assay and inter-assay precision was studied at three and four concentration levels, respectively, and was less than 19% for all compounds. Accuracy was also satisfactory for all. An excellent linearity was observed from the LOQs up to 1000 mug/l for milnacipram and paroxetine and from each LOQ up to 400 mg/l for the other compounds. The performance of the methods described thus allows the therapeutic drug monitoring of the currently commercialised SSRIs.

L32 ANSWER 21 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:246515 BIOSIS Full-text
DOCUMENT NUMBER: PREV200000246515
TITLE: Development of a simple in-vial liquid-phase

microextraction device for drug analysis compatible with capillary gas chromatography, capillary electrophoresis and high-performance liquid chromatography.

AUTHOR(S): Rasmussen, Knut Einar; Pedersen-Bjergaard, Stig [Reprint author]; Krogh, Mette; Ugland, Hege Grefslie; Gronhaug, Trine

CORPORATE SOURCE: School of Pharmacy, University of Oslo, Blindern, 0316, Oslo, Norway

SOURCE: Journal of Chromatography A, (March 17, 2000) Vol. 873, No. 1, pp. 3-11. print.
CODEN: JOCRAM. ISSN: 0021-9673.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 14 Jun 2000
Last Updated on STN: 5 Jan 2002

AB A simple, inexpensive and disposable device for liquid-phase microextraction (LPME) is presented for use in combination with capillary gas chromatography (GC), capillary electrophoresis (CE) and high-performance liquid chromatography (HPLC). 1-4 ml samples of human urine or plasma were filled into conventional 4-ml vials, whereafter 15-25 mul of the extraction medium (acceptor solution) was filled into a short piece of a porous hollow fiber and placed into the sample vial. The drugs of interest were extracted from the sample solutions and into the small volumes of acceptor solution based on high partition coefficients and were preconcentrated by a factor of 30-125. For LPME in combination with GC, the porous hollow fiber was filled with 15 mul n-octanol as the acceptor solution. Following 30 min of extraction, the organic acceptor solution was injected directly into the GC system. For LPME in combination with CE and HPLC, n-octanol was immobilized within the pores of the hollow fiber, while the internal volume of the fiber was filled with either 25 mul of 0.1 M HCl (for extraction of basic compounds) or 25 mul 0.02 M NaOH (for acidic compounds). Following 45 min extraction, the aqueous acceptor solution was injected directly into the CE or HPLC system. Owing to the low cost, the extraction devices were disposed after a single extraction which eliminated the possibility of carry over effects. In addition, because no expensive instrumentation was required for LPME, 10-30 samples were extracted in parallel to provide a high number of samples per unit time capacity.

L32 ANSWER 22 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:92356 BIOSIS Full-text

DOCUMENT NUMBER: PREV200100092356

TITLE: Biophysical characterization of the cocaine binding crevice in the purified serotonin transporter using a fluorescent cocaine analogue.

AUTHOR(S): Rasmussen, S. G. [Reprint author]; Jensen, A. D.; Carrol, I.; Granas, C. C.; Tate, C. G.; Gether, U.

CORPORATE SOURCE: University of Copenhagen, Copenhagen, Denmark

SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-438.8. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 04-09, 2000. Society for Neuroscience.
ISSN: 0190-5295.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 21 Feb 2001
Last Updated on STN: 12 Feb 2002

AB The rat serotonin transporter (rSERT) was expressed in Sf-9 insect cells, solubilized in digitonin and purified using nickel chromatography followed by Concanavalin A chromatography to select for glycosylated and correctly folded rSERT. The pharmacological properties of the purified transporter were similar to that of the transporter in Sf-9 cell membranes with unchanged affinities for 5-HT, RTI-55 and citalopram. To explore the biophysical properties of the still unknown cocaine-binding site, a high affinity cocaine-analogue (RTI-233; KI simeq 60 nM), which contained the environmentally sensitive fluorescent NBD-moiety, was synthesized. Specific binding of RTI-233 to the purified rSERT was evidenced by measurement of fluorescence anisotropy demonstrating constrained mobility of bound RTI-233 in comparison to free RTI-233. The fluorescence of bound RTI-233 displayed an emission maximum (lambdaMAX) of 532 nm corresponding to a 4 nm blue-shift as compared to lambdaMAX of RTI-233 in aqueous solution and corresponding to the lambdaMAX of RTI-233 in 80% dioxane. Collisional quenching experiments revealed that the aqueous quencher potassium iodide (KI) was able to quench the fluorescence of RTI-233 in the cocaine binding pocket although not to the same extent as free RTI-233. Conversely, the hydrophobic quencher TEMPO quenched the fluorescence of bound RTI-233 more efficiently than free RTI-233. In conclusion, our data provide the first insight into the biophysical character of the cocaine binding site, revealing a highly hydrophobic but partially water-exposed binding pocket in the rSERT.

L32 ANSWER 23 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:68416 BIOSIS Full-text
DOCUMENT NUMBER: PREV200000068416
TITLE: Simultaneous determination of citalopram, fluoxetine, paroxetine and their metabolites in plasma and whole blood by high-performance liquid chromatography with ultraviolet and fluorescence detection.
AUTHOR(S): Kristoffersen, L. [Reprint author]; Bugge, A.; Lundanes, E.; Slordal, L.
CORPORATE SOURCE: National Institute of Forensic Toxicology, N-0105, Oslo, Norway
SOURCE: Journal of Chromatography B, (Nov. 12, 1999) Vol. 734, No. 2, pp. 229-246. print.
CODEN: JCBADL. ISSN: 0378-4347.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Feb 2000
Last Updated on STN: 3 Jan 2002

AB A method for the simultaneous determination of the three selective serotonin reuptake inhibitors (SSRIs) citalopram, fluoxetine, paroxetine and their metabolites in whole blood and plasma was developed. Sample clean-up and separation were achieved using a solid-phase extraction method with C8 non-endcapped columns followed by reversed-phase high-performance liquid chromatography with fluorescence and ultraviolet detection. The robustness of the solid-phase extraction method was tested for citalopram, fluoxetine, paroxetine, Cl-citalopram and the internal standard, protriptyline, using a fractional factorial design with nine factors at two levels. The fractional factorial design showed two significant effects for paroxetine in whole blood. The robustness testing for citalopram, fluoxetine, Cl-citalopram and the internal standard revealed no significant main effects in whole blood and plasma. The optimization and the robustness of the high-performance liquid chromatographic separation were investigated with regard to pH and relative amount of acetonitrile in the mobile phase by a central composite design circumscribed. No alteration in the elution order and no significant change in resolution for a deviation of +-1% acetonitrile and +-0.3 pH units from the

specified conditions were observed. The method was validated for the concentration range 0.050-5.0 mumol/l with fluorescence detection and 0.12-5.0 mumol/l with ultraviolet detection. The limits of quantitation were 0.025 mumol/l for citalopram and paroxetine, 0.050 mumol/l for desmethyl citalopram, di-desmethyl citalopram and citalopram-N-oxide, 0.12 mumol/l for the paroxetine metabolites by fluorescence detection, and 0.10 mumol/l for fluoxetine and norfluoxetine by ultraviolet detection. Relative standard deviations for the within-day and between-day precision were in the ranges 1.4-10.6% and 3.1-20.3%, respectively. Recoveries were in the 63-114% range for citalopram, fluoxetine and paroxetine, and in the 38-95% range for the metabolites. The method has been used for the analysis of whole blood and plasma samples from SSRI-exposed patients and forensic cases.

L32 ANSWER 24 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1998:355968 BIOSIS Full-text
DOCUMENT NUMBER: PREV199800355968
TITLE: Simultaneous determination of human plasma levels of citalopram, paroxetine, sertraline, and their metabolites by gas chromatography-mass spectrometry.
AUTHOR(S): Eap, C. B. [Reprint author]; Bouchoux, G.; Cochard, M. Amey,n.; Savary, L.; Baumann, P.
CORPORATE SOURCE: Unite Biochim. Psychopharmacol. Clin., Dep. Universitaire Psychiatrie Adulte, Hop. Cery, CH-1008 Prilly-Lausanne, Switzerland
SOURCE: Journal of Chromatographic Science, (July, 1998) Vol. 36, No. 7, pp. 365-371. print.
CODEN: JCHSBZ. ISSN: 0021-9665.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Aug 1998
Last Updated on STN: 21 Oct 1998

AB A gas chromatography-mass spectrometry method is presented which allows the simultaneous determination of the plasma concentrations of the selective serotonin reuptake inhibitors citalopram, paroxetine, sertraline, and their pharmacologically active N-demethylated metabolites (desmethylcitalopram, didesmethylcitalopram, and desmethylsertraline) after derivatization with the reagent N-methyl-bis(trifluoroacetamide). No interferences from endogenous compounds are observed following the extraction of plasma samples from six different human subjects. The standard curves are linear over a working range of 10-500 ng/mL for citalopram, 10-300 ng/mL for desmethylcitalopram, 5-60 ng/mL for didesmethylcitalopram, 20-400 ng/mL for sertraline and desmethylsertraline, and 10-200 ng/mL for paroxetine. Recoveries measured at three concentrations range from 81 to 118% for the tertiary amines (citalopram and the internal standard methylmaprotiline), 73 to 95% for the secondary amines (desmethylcitalopram, paroxetine and sertraline), and 39 to 66% for the primary amines (didesmethylcitalopram and desmethylsertraline). Intra- and interday coefficients of variation determined at three concentrations range from 3 to 11% for citalopram and its metabolites, 4 to 15% for paroxetine, and 5 to 13% for sertraline and desmethylsertraline. The limits of quantitation of the method are 2 ng/mL for citalopram and paroxetine, 1 ng/mL for sertraline, and 0.5 ng/mL for desmethylcitalopram, didesmethylcitalopram, and desmethylsertraline. No interferences are noted from 20 other psychotropic drugs. This sensitive and specific method can be used for single-dose pharmacokinetics. It is also useful for therapeutic drug monitoring of these three drugs and could possibly be adapted for the quantitation of the two other selective serotonin reuptake inhibitors on the market, namely fluoxetine and fluvoxamine.

L32 ANSWER 25 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:12863 BIOSIS Full-text
DOCUMENT NUMBER: PREV199900012863
TITLE: Analysis of the enantiomers of citalopram and its demethylated metabolites using chiral liquid chromatography.
AUTHOR(S): Kosel, M.; Eap, C. B.; Amey, M.; Baumann, P. [Reprint author]
CORPORATE SOURCE: DUPA-Hopital Cery, CH-1008 Prilly-Lausanne, Switzerland
SOURCE: Journal of Chromatography B, (Nov. 20, 1998) Vol. 719, No. 1-2, pp. 234-238. print.
CODEN: JCBADL. ISSN: 0378-4347.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jan 1999
Last Updated on STN: 11 Jan 1999

AB A procedure using a chirobiotic V column is presented which allows separation of the enantiomers of citalopram and its two N-demethylated metabolites, and of the internal standard, alprenolol, in human plasma. Citalopram, demethylcitalopram and didemethylcitalopram, as well as the internal standard, were recovered from plasma by liquid-liquid extraction. The limits of quantification were found to be 5 ng/ml for each enantiomer of citalopram and demethylcitalopram, and 7.5 ng/ml for each enantiomer of didemethylcitalopram. Inter- and intra-day coefficients of variation varied from 2.4% to 8.6% for Sand R-citalopram, from 2.9% to 7.4% for S- and R-demethylcitalopram, and from 5.6% to 12.4% for S- and R-didemethylcitalopram. No interference was observed from endogenous compounds following the extraction of plasma samples from 10 different patients treated with citalopram. This method allows accurate quantification for each enantiomer and is, therefore, well suited for pharmacokinetic and drug interaction investigations. The presented method replaces a previously described highly sensitive and selective high-performance liquid chromatography procedure using an acetylated beta-cyclobond column which, because of manufactural problems, is no longer usable for the separation of the enantiomers of citalopram and its demethylated metabolites.

L32 ANSWER 26 OF 33 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 96082510 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7581865
TITLE: Simultaneous determination of citalopram and its metabolites by high-performance liquid chromatography with column switching and fluorescence detection by direct plasma injection.
AUTHOR: Matsui E; Hoshino M; Matsui A; Okahira A
CORPORATE SOURCE: Central Research Laboratories, Zeria Pharmaceutical Co., Ltd., Saitama, Japan.
SOURCE: Journal of chromatography. B, Biomedical applications, (1995 Jun 23) Vol. 668, No. 2, pp. 299-307.
Journal code: 9421796. ISSN: 0378-4347.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 24 Jan 1996
Last Updated on STN: 24 Jan 1996
Entered Medline: 12 Dec 1995

AB High-performance liquid chromatography with a successive column-switching technique was developed for simultaneous determination of citalopram and its four metabolites in plasma. Plasma samples were injected directly, and the target compounds were purified and concentrated with an inexpensive commercial octadecyl guard column. Then, the six-port valve was switched, and the compounds retained in the column were eluted by the back-flush method using 20 mM phosphate buffer (pH 4.6)-acetonitrile (70:30, v/v) containing 0.1% diethylamine and separated with an ODS column. The compounds were assayed with a fluorescence detector at an excitation wavelength of 249 nm and an emission wavelength of 302 nm. At least 30 plasma samples could be treated with an octadecyl guard column. The limits of quantitation of this method were 2.0 ng/ml for citalopram, desmethylcitalopram, didesmethylcitalopram, citalopram propionic acid and citalopram N-oxide. This method was applied to a pharmacokinetic study in dogs and a toxicokinetic study in rats.

L32 ANSWER 27 OF 33 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 92296047 EMBASE Full-text
DOCUMENT NUMBER: 1992296047
TITLE: Partial purification and characterization of the sodium-ion-coupled 5-hydroxytryptamine transporter of rat cerebral cortex.
AUTHOR: Graham D.; Esnaud H.; Langer S.Z.
CORPORATE SOURCE: Synthelabo Recherche (LERS), 31 avenue Paul Vaillant Couturier,F-92220 Bagneux, France
SOURCE: Biochemical Journal, (1992) Vol. 286, No. 3, pp. 801-805. ISSN: 0264-6021 CODEN: BIJOAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 25 Oct 1992
Last Updated on STN: 25 Oct 1992

AB A procedure for the extensive purification of the Na+-coupled 5-hydroxytryptamine transporter of rat cerebral cortex has been developed. The 5-hydroxytryptamine transporter was solubilized with the non-ionic detergent digitonin, and the detergent extracts were subjected to sequential affinity chromatography on a citalopram-based agarose support and wheat-germ-agglutinin-Sepharose. 5-Hydroxytryptamine transporters in the affinity-purified preparation were identified by using the selective 5-hydroxytryptamine-uptake inhibitor [3H]paroxetine, and were shown to display a similar pharmacological profile to those present in particulate preparations. An overall transporter purification of around 2000-fold was achieved with a 9% recovery. SDS/PAGE of affinity-chromatographed material starting from detergent extracts incubated in the presence or absence of 1 mM-citalopram indicated that a polypeptide of M(r) 73000 corresponded to the S-hydroxytryptamine- transporter protein.

L32 ANSWER 28 OF 33 MEDLINE on STN

ACCESSION NUMBER: 90241914 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2334696
TITLE: Partial purification of the 5-hydroxytryptamine-reuptake system from human blood platelets using a citalopram-derived affinity resin [corrected].
AUTHOR: Biessen E A; Horn A S; Robillard G T

CORPORATE SOURCE: Department of Physical Chemistry, University of Groningen, The Netherlands.
SOURCE: Biochemistry, (1990 Apr 3) Vol. 29, No. 13, pp. 3349-54. Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199006
ENTRY DATE: Entered STN: 6 Jul 1990
Last Updated on STN: 6 Jul 1990
Entered Medline: 12 Jun 1990

AB This paper describes a procedure for the synthesis and application of a citalopram-derived affinity resin in purifying the 5HT-reuptake system from human blood platelets. A two-step scheme has been developed for partial purification, based on wheat germ agglutinin-lectin (WGA) affinity and citalopram affinity chromatographies. Upon solubilization of the carrier with 1% digitonin, a 50-70-fold increase in specific [3H]imipramine binding activity with a 70% recovery could be accomplished through WGA-lectin chromatography. The WGA pool was then subjected to affinity chromatography on citalopram-agarose. At least 90% of the binding capacity adsorbed to the column. Specific elution using 10 microM citalopram resulted in a 22% recovery of binding activity. A 10,000-fold overall purification was obtained by using this two-step procedure. Analysis of the fractions on SDS-PAGE after 125I labeling revealed specific elution of 78- and 55-kDa proteins concomitant with the appearance of [3H]imipramine binding activity. The pharmacological profile of the partially purified reuptake system correlated well with that derived from the crude membrane-bound reuptake system, suggesting a copurification of the 5HT binding activity and [3H]imipramine binding activity.

L32 ANSWER 29 OF 33 EMBASE
ACCESSION NUMBER: 90388317 EMBASE Full-text
DOCUMENT NUMBER: 1990388317
TITLE: Preparation and characterization of anti-paroxetine antibodies.
AUTHOR: Strijewski A.; Tang S.W.
CORPORATE SOURCE: Psychopharmacology Unit, Clarke Institute of Psychiatry, Toronto, Ont., Canada
SOURCE: Life Sciences, (1990) Vol. 47, No. 14, pp. 1213-1219. . ISSN: 0024-3205 CODEN: LIFSAK
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
032 Psychiatry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 1991
Last Updated on STN: 13 Dec 1991

AB 6-Nitroparoxetine was synthesized and reduced to 6-aminoparoxetine. After coupling to glutaraldehyde at the 6-position and to bovine serum albumin, the resulting Schiff's base was further reduced into an amino-derivative which served as the antigen. Anti-paroxetine antibodies were raised against this antigen in rabbits and the anti-paroxetine IgG purified by Protein A affinity

chromatography. The antiparoxetine IgG demonstrated high specificity towards paroxetine and 6-nitroparoxetine without significant cross-reactivity with other commonly used antidepressant and neuroleptic drugs. These antibodies may be useful for both plasma paroxetine level assays and uptake inhibitor binding site studies.

L32 ANSWER 30 OF 33 MEDLINE on STN
ACCESSION NUMBER: 90299654 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2163372
TITLE: Synthesis of a selective serotonin uptake inhibitor: [11C]citalopram.
AUTHOR: Dannals R F; Ravert H T; Wilson A A; Wagner H N Jr
CORPORATE SOURCE: Division of Nuclear Medicine, Johns Hopkins Medical Institutions, Baltimore, MD 21205-2179.
CONTRACT NUMBER: CA-32845 (NCI)
NS-15080 (NINDS)
SOURCE: International journal of radiation applications and instrumentation. Part A, Applied radiation and isotopes, (1990) Vol. 41, No. 6, pp. 541-3.
Journal code: 8611097. ISSN: 0883-2889.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199008
ENTRY DATE: Entered STN: 7 Sep 1990
Last Updated on STN: 7 Sep 1990
Entered Medline: 7 Aug 1990

AB Citalopram, a selective serotonin uptake inhibitor, was labeled with 11C for non-invasive in vivo studies of serotonin uptake sites in the human brain using positron emission tomography. The synthesis was completed in approximately 17 min using [11C]methyl iodide as the precursor. The synthesis, purification, characterization, and determination of specific activity are described.

L32 ANSWER 31 OF 33 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 4
ACCESSION NUMBER: 1990:475483 BIOSIS Full-text
DOCUMENT NUMBER: PREV199090114903; BA90:114903
TITLE: SEROTONIN TRANSPORT SYSTEMS AND ANTIDEPRESSANTS.
AUTHOR(S): GALZIN A M [Reprint author]; GRAHAM D; LANGER S Z
CORPORATE SOURCE: SYNTHELABO RECHERCHE, 58 RUE DE LA GLACIERE, 75013 PARIS, FRANCE
SOURCE: Psychiatrie and Psychobiologie, (1990) Vol. 5, No. 3, pp. 201-208.
ISSN: 0767-399X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: FRENCH
ENTRY DATE: Entered STN: 25 Oct 1990
Last Updated on STN: 25 Oct 1990

AB The sodium-dependent serotonin transport associated with plasmatic membranes of platelets or serotonin nerve terminals serves to inactive the neurotransmitter and maintain low levels of transmitter in the synaptic cleft. It has been suggested that changes in serotonergic transmission could be linked to the pathophysiology of depression, and that modifications at the level of the serotonin transporter could exist during depressive episodes. A

consistent decrease in the number of transporter sites has been reported in blood platelets from depressed patients, and similar results were also obtained in some regions of the post-mortem human brain. It is well established that tricyclic and nontricyclic serotonin uptake inhibitors are effective as antidepressant drugs, but a lag period of 2-3 wks is observed between the beginning of treatment and the clinical manifestation of therapeutic antidepressant effects. Therefore, studies on biochemical properties and molecular characterization of the serotonin transporter are of particular interest. Serotonin uptake can be selectively inhibited by citalopram, paroxetine, indalpine, fluoxetine and SL 81 0385. Moreover, this inhibition by paroxetine and SL 81 0385 has been shown to induce an increase in the electrically-evoked in vitro release of [3H]-5-HT from slices of the human frontal cortex. Radioligand binding studies with [3H]-impiramine, [3H]-paroxetine and [3H]-citalopram has been used in recent years to characterize the serotonin transporter. In dissociation kinetics experiments of [3H]-paroxetine binding to rat cerebral cortical membranes, exposure to citalopram, indalpine, fluoxetine, SL 81 0385, imipramine as well as serotonin itself produced monophasic dissociation curves with t 1/2 values of dissociation similar to that obtained for paroxetine itself. Moreover, SL 810385, fluoxetine, imipramine and serotonin can protect [3H]-paroxetine binding against N-ethylmaleimide-induced inactivation. Combined, these results suggest that the substrate and the tricyclic and nontricyclic serotonin uptake inhibitors bind to the same (or at least overlapping) domains on the sodium-coupled serotonin transporter. The neuronal serotonin transporter has been solubilized from rat cerebral cortex membranes, and purified by affinity chromatography using an agarose gel to which a citalopram derivative had been covalently coupled. [3H]-paroxetine binding to a purified preparation gave a Kd value of 0.71 nM and a value of Bmax greater than 1.962 pmoles/mg prot, corresponding to an enrichment of more than 3000-fold of [3H]-paroxetine binding activity compared to that of the parent membrane preparation. The binding of [3H]paroxetine to this purified preparation was inhibited by citalopram, imipramine and serotonin with Ki values of 19 nM, 80 nM and 3.5 µM, respectively, thereby confirming than an extensive purification of the sodium-coupled serotonin transporter had been achieved. This purification of the 5-HT carrier protein is the first step which should ultimately permit a detailed insight into the molecular mechanisms operating in this transport process.

L32 ANSWER 32 OF 33 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER:	86207093 EMBASE Full-text
DOCUMENT NUMBER:	1986207093
TITLE:	Solubilization and characterization of the 5-hydroxytryptamine transporter complex from rat cerebral cortical membranes.
AUTHOR:	Habert E.; Graham D.; Langer S.Z.
CORPORATE SOURCE:	Laboratoires d'Etudes et de Recherches Synthelabo (LERS), 75013 Paris, France
SOURCE:	European Journal of Pharmacology, (1986) Vol. 122, No. 2, pp. 197-204. . CODEN: EJPHAZ
COUNTRY:	Netherlands
DOCUMENT TYPE:	Journal
FILE SEGMENT:	037 Drug Literature Index 030 Pharmacology 008 Neurology and Neurosurgery
LANGUAGE:	English
ENTRY DATE:	Entered STN: 10 Dec 1991 Last Updated on STN: 10 Dec 1991

AB The 5-hydroxytryptamine transporter complex from rat cerebral cortical membranes was solublized with digitonin. The affinity of the solubilized transporter complex for [3H]paroxetine, a very selective and potent inhibitor of 5-hydroxytryptamine uptake, was not affected and remained unchanged when compared with the parent membrane preparation. The solubilization yield of membrane-bound [3H]paroxetine binding sites was 42%. The pharmacological profile of the solubilized transporter complex was similar to that of the intact transporter in membranes of the cerebral cortex, with the exception of tryptamine, which exhibited a 10-fold loss in potency to inhibit [3H]paroxetine binding to the solubilized transporter when compared to membranes. The Stokes radius determined by gel filtration was 7.6 nm. This successful solubilization of the neuronal 5-hydroxytryptamine transporter complex is the starting point for purification of this macromolecular moiety.

L32 ANSWER 33 OF 33 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 82120398 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6948816
TITLE: Determination of the antidepressant agent citalopram and metabolites in plasma by liquid chromatography with fluorescence detection.
AUTHOR: Oyehaug E; Ostensen E T; Salvesen B
SOURCE: Journal of chromatography, (1982 Jan 8) Vol. 227, No. 1, pp. 129-35.
Journal code: 0427043. ISSN: 0021-9673.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198204
ENTRY DATE: Entered STN: 17 Mar 1990
Last Updated on STN: 17 Mar 1990
Entered Medline: 12 Apr 1982

AB A high-performance liquid chromatographic method is described for the determination of citalopram [1-(3-(dimethylaminopropyl)-1-(4- fluorophenyl)-5-phthalancarbonitrile] and its two main metabolites (the methylamino and amino derivatives). The compounds were extracted from alkaline plasma with diethyl ether. The combined ether layers were evaporated after addition of 50 microliter of 0.1 N HCl. The residual extracts were purified with diethyl ether and 20 microliter were injected into a Spherisorb ODS 5-micrometer column with acetonitrile--0.6% phosphate buffer pH 3 (55:45, v/v) as the mobile phase. Using a fluorescence detector the detection limits are 1 ng/ml of plasma for citalopram and the methylamino metabolite and 0.5 ng/ml for the amino metabolite.

FILE 'CAPLUS' ENTERED AT 18:17:07 ON 19 SEP 2007

FILE COVERS 1907 - 19 Sep 2007 VOL 147 ISS 13
FILE LAST UPDATED: 18 Sep 2007 (20070918/ED)

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http://www.cas.org/infopolicy.html

L33 62 L16 AND L21

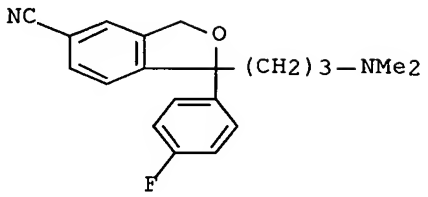
=> s l33 and pd<dec 2003
23856944 PD<DEC 2003
(PD<20031200)
L34 31 L33 AND PD<DEC 2003

=> d 1-31 ibib abs hitstr;s mei r?/au;s guo d?/au;s wang s?/au

L34 ANSWER 1 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:941048 CAPLUS Full-text
DOCUMENT NUMBER: 143:248272
TITLE: Preparation of citalopram hydrobromide
INVENTOR(S): Wang, Chaoyang; He, Shunchao; Huang, Yaozong; Lin, Fengru; Zhou, Zhongyin; Liang, Long; Cheng, Zhipeng
PATENT ASSIGNEE(S): Sichuan Kelun Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 6 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

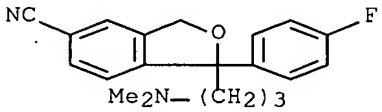
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1440968	A	20030910	CN 2003-117564	20030331 <--
PRIORITY APPLN. INFO.:			CN 2003-117564	20030331

AB The method comprises salifying citalopram with 40-65% aqueous HBr solution in organic solvent (Et ether, iso-Pr ether, THF, etc) at 10-40°, concentrating to recover organic solvent, and crystallizing at 0-20° for 6-12 h.
IT 59729-32-7P, Citalopram hydrobromide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of citalopram hydrobromide by salt formation with aqueous HBr)
RN 59729-32-7 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



● HBr

IT 59729-33-8, Citalopram
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of citalopram hydrobromide by salt formation with aqueous HBr)
RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



L34 ANSWER 2 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:991182 CAPLUS Full-text
DOCUMENT NUMBER: 140:31501
TITLE: Crystals of pharmaceutically acceptable salts of citalopram, methods of crystallization, and pharmaceutical compositions comprising them
INVENTOR(S): Liljegren, Ken; Holm, Per; Nielsen, Ole; Wagner, Sven
PATENT ASSIGNEE(S): H. Lundbeck A/s, Den.
SOURCE: U.S. Pat. Appl. Publ., 7 pp., Cont.-in-part of U.S. Ser. No. 730,380.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003232881	A1	20031218	US 2002-310621	20021205
US 2003109577	A1	20030612	US 2000-730380	20001205 <--
US 6849659	B2	20050201		
GB 2376233	A	20021211	GB 2002-19820	20010731 <--
GB 2376233	B	20030910		
US 2005053652	A1	20050310	US 2004-966725	20041015

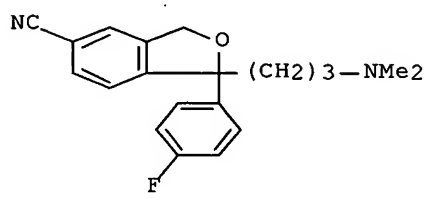
PRIORITY APPLN. INFO.:

DK 2000-1614	A	20001027
US 2000-730380	A2	20001205
DK 2000-1202	A	20000810
GB 2001-18579	A3	20010731

AB A method of crystallizing larger particles of citalopram or its hydrochloride or hydrobromide, in a size comparable to the size of the filler which are useful for the manufacture of directly compressed tablets is presented.

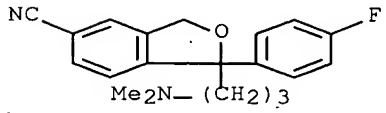
IT 59729-32-7P, Citalopram hydrobromide 59729-33-8P, Citalopram 85118-27-0P, Citalopram hydrochloride
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(crystallization process for the preparation of larger crystals of)

RN 59729-32-7 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)

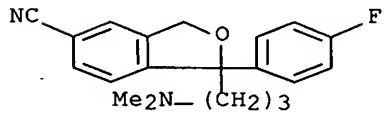


● HBr

RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



RN 85118-27-0 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

L34 ANSWER 3 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:777773 CAPLUS Full-text
DOCUMENT NUMBER: 139:276808
TITLE: Transalification process for the preparation of purified citalopram hydrochloride or hydrobromide

INVENTOR(S): Hamied, Yusuf Khwaja; Kankan, Rajendra N.; Rao, Dharmaraj R.
PATENT ASSIGNEE(S): Cipla Ltd., India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080589	A1	20031002	WO 2003-GB1032	20030311 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003212524	A1	20031008	AU 2003-212524	20030311 <--
EP 1485367	A1	20041215	EP 2003-708344	20030311
EP 1485367	B1	20070801		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008603	A	20050209	BR 2003-8603	20030311
IN 2004MN00550	A	20060505	IN 2004-MN550	20041001
PRIORITY APPLN. INFO.:			GB 2002-6708 A	20020321
			WO 2003-GB1032 W	20030311

AB Purified citalopram hydrochloride or hydrobromide are made by purifying another different citalopram salt (e.g., citalopram besylate by crystallization) and then converting the purified salt to the hydrochloride or hydrobromide.

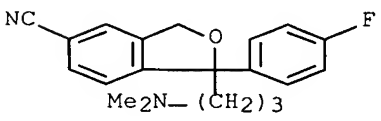
IT 606932-12-1P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(transalification process for the preparation of purified citalopram hydrochloride or hydrobromide)

RN 606932-12-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monobenzenesulfonate (9CI) (CA INDEX NAME)

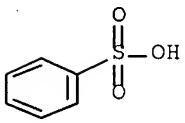
CM 1

CRN 59729-33-8
CMF C20 H21 F N2 O

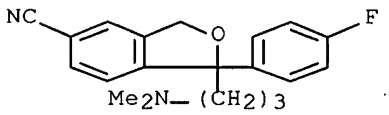


CM 2

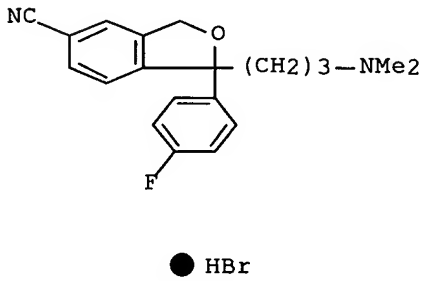
CRN 98-11-3
CMF C6 H6 O3 S



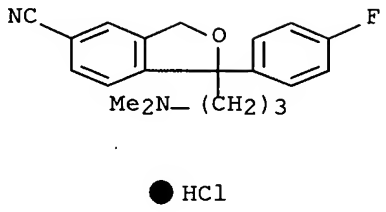
IT 59729-33-8, Citalopram
RL: RCT (Reactant); RACT (Reactant or reagent)
(transalification process for the preparation of purified citalopram hydrochloride or hydrobromide)
RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



IT 59729-32-7P, Citalopram hydrobromide 85118-27-0P, Citalopram hydrochloride
RL: SPN (Synthetic preparation); PREP (Preparation)
(transalification process for the preparation of purified citalopram hydrochloride or hydrobromide)
RN 59729-32-7 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



RN 85118-27-0 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrochloride (1:1) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 4 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:752685 CAPLUS Full-text
DOCUMENT NUMBER: 139:261161
TITLE: Improved process for the preparation of citalopram and its hydrobromide
INVENTOR(S): Babu, Ambati Narahari; Goud, Vuddamari Srinivas; Gaonkar, Santhosh Laxman; Thomas, Saji D.; Manjunatha, Sulur G.; Kulkami, Ashok Krishna
PATENT ASSIGNEE(S): Jubilant Organosys Limited, India
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1346989	A1	20030924	EP 2002-252047	20020321 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
WO 2003080590	A1	20031002	WO 2003-IB1641	20030321 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003219423	A1	20031008	AU 2003-219423	20030321 <--
US 2005217562	A1	20051006	US 2005-508529	20050610
US 7255741	B2	20070814		

PRIORITY APPLN. INFO.: EP 2002-252047 A 20020321
WO 2003-IB1641 W 20030321
OTHER SOURCE(S): CASREACT 139:261161

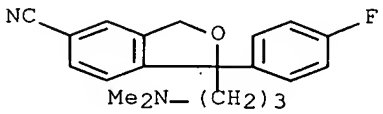
AB A process for the preparation of citalopram (an anti-depressant drug) comprises the C-alkylation of 1-(4-fluorophenyl)-1,3-dihydroisobenzofuran- 5-carbonitrile (5-cyanophthalane) with 3-dimethylaminopropyl chloride in the presence of potassium tert.-butoxide. Suitably, the alkylation is carried out in the presence of DMSO (DMSO). The citalopram thereby produced can be isolated as a crystalline solid in one step from the reaction mixture by adding an equal volume of a water-miscible solvent, such as iso-Pr alc., to

the mixture Citalopram hydrobromide is prepared by treating citalopram (base) with aqueous hydrobromic acid, such as at pH 1-3.

IT 59729-33-8P, Citalopram
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(improved process for the preparation of citalopram and its hydrobromide)

RN 59729-33-8 CAPLUS

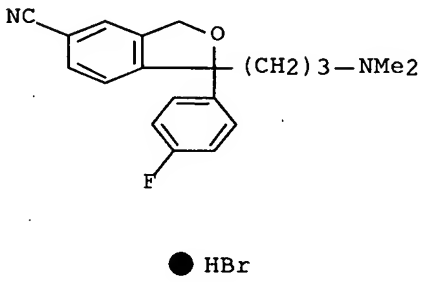
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



IT 59729-32-7P, Citalopram hydrobromide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(improved process for the preparation of citalopram and its hydrobromide)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 5 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:696884 CAPLUS Full-text

DOCUMENT NUMBER: 139:230614

TITLE: Adsorption-washing-desorption process for the purification of citalopram

INVENTOR(S): Hamied, Yusuf Khwaja; Kankan, Rajendra N.; Rao, Dharmaraj R.

PATENT ASSIGNEE(S): Cipla Ltd., India; Wain, Christopher Paul

SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

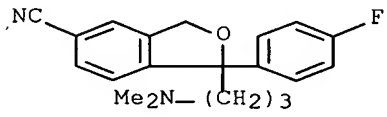
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072564	A1	20030904	WO 2003-GB836	20030227 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
GB 2386119	A	20030910	GB 2002-4682	20020227 <--
AU 2003208456	A1	20030909	AU 2003-208456	20030227 <--
EP 1478638	A1	20041124	EP 2003-706744	20030227
EP 1478638	B1	20060809		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008062	A	20041228	BR 2003-8062	20030227
PRIORITY APPLN. INFO.:			GB 2002-4682 A	20020227
			WO 2003-GB836 W	20030227

AB Crude citalopram base is purified by adsorption on a solid support (e.g., Celite), washing the support-adsorbed citalopram to selectively remove impurities with an aliphatic-aromatic hydrocarbon solvent mixture (e.g., hexane and toluene), and desorbing the purified base from the support by contact with a polar solvent (e.g., Et acetate). The purified citalopram is then salified with an acid (e.g., aqueous hydrogen bromide) to produce a pharmaceutically acceptable citalopram salt (e.g., citalopram hydrobromide).

IT 59729-33-8P, Citalopram
RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); RCT (Reactant); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(adsorption-washing-desorption process for the purification of citalopram)

RN 59729-33-8 CAPLUS

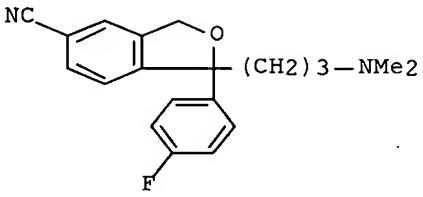
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



IT 59729-32-7P, Citalopram hydrobromide
RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(salification of citalopram base with acids in the preparation of pharmaceutically acceptable citalopram salts)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



● HBr

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 6 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:696883 CAPLUS Full-text
DOCUMENT NUMBER: 139:214318
TITLE: Chromatographic process for the purification of amorphous citalopram and the preparation of citalopram salts
INVENTOR(S): Hamied, Yusuf Khwaja; Kankan, Rajendra N.; Rao, Dharmaraj R.
PATENT ASSIGNEE(S): Cipla Ltd., India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072562	A1	20030904	WO 2003-GB810	20030226 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
GB 2386118	A	20030910	GB 2002-4680	20020227 <--
AU 2003207348	A1	20030909	AU 2003-207348	20030226 <--
EP 1478636	A1	20041124	EP 2003-704820	20030226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008060	A	20041228	BR 2003-8060	20030226
IN 2004MN00542	A	20050520	IN 2004-MN542	20040930

PRIORITY APPLN. INFO.: GB 2002-4680 A 20020227
WO 2003-GB810 W 20030226

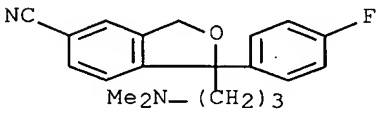
AB Citalopram base is purified and isolated by chromatog. techniques and then subjected to spray drying and salification with aqueous HBr for the preparation of citalopram hydrobromide.

IT 59729-33-8P, Citalopram
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PUR (Purification or recovery); PYP (Physical process); RCT (Reactant); PREP

(Preparation); PROC (Process); RACT (Reactant or reagent)
(chromatog. process for the purification of amorphous citalopram and the preparation of citalopram salts)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)

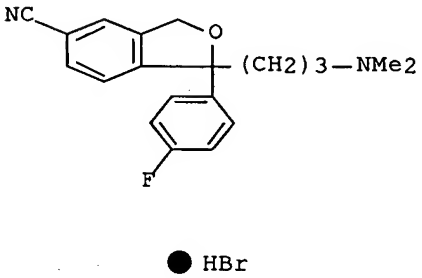


IT 59729-32-7P, Citalopram hydrobromide

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(chromatog. process for the purification of amorphous citalopram and the preparation of citalopram salts)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 7 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:590880 CAPLUS Full-text

DOCUMENT NUMBER: 139:133459

TITLE: Cyanation process for the preparation of citalopram and its extractive purification

INVENTOR(S): Coppi, Laura; Gasanz Guillen, Yolanda; Campon Pardo, Julio

PATENT ASSIGNEE(S): Esteve Quimica, S.A., Spain

SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003144534	A1	20030731	US 2003-351289	20030124 <--
US 6635773	B2	20031021		

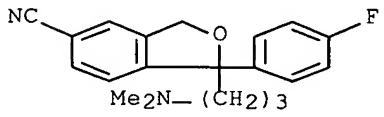
ES 2194597	A1	20031116	ES 2002-167	20020125 <--
ES 2194597	B2	20040801		
CA 2474323	A1	20030731	CA 2003-2474323	20030124 <--
WO 2003062218	A1	20030731	WO 2003-ES37	20030124 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1479673	A1	20041124	EP 2003-706634	20030124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005522419	T	20050728	JP 2003-562097	20030124
CN 1688565	A	20051026	CN 2003-802625	20030124
ZA 2004005441	A	20050708	ZA 2004-5441	20040708
IN 2004KN00960	A	20060505	IN 2004-KN960	20040708
MX 2004PA07156	A	20041029	MX 2004-PA7156	20040723
NO 2004003568	A	20040825	NO 2004-3568	20040825
PRIORITY APPLN. INFO.:			ES 2002-167 A	20020125
			WO 2003-ES37 W	20030124

AB Crude citalopram was prepared the cyanation of 1-[3-(dimethylamine)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5- bromoisobenzofuran with copper cyanide and purified citalopram or one of its salts (e.g., citalopram hydrobromide) was obtained by the extractive purification of citalopram by selective extns. of citalopram or it salts of its impurities with organic solvents (e.g., toluene and heptane) and water under specific conditions of pH and temperature

IT 59729-33-8P, Citalopram
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(cyanation process for the preparation of citalopram and its extractive purification)

RN 59729-33-8 CAPLUS

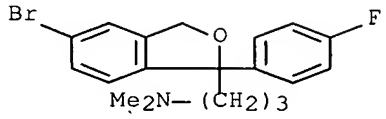
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



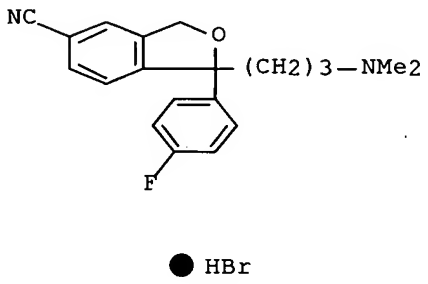
IT 64169-39-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyanation process for the preparation of citalopram and its extractive purification)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (CA INDEX NAME)



IT 59729-32-7P, Citalopram hydrobromide
RL: SPN (Synthetic preparation); PREP (Preparation)
(cyanation process for the preparation of citalopram and its extractive purification)
RN 59729-32-7 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)

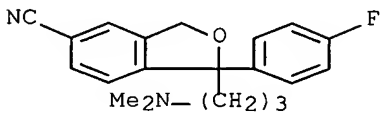


L34 ANSWER 8 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:559857 CAPLUS Full-text
DOCUMENT NUMBER: 139:101019
TITLE: Preparation of high-purity citalopram and its acid salts from 1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile and 3-(dimethylamino)propyl chloride
INVENTOR(S): Arai, Nobuhiro; Ikemoto, Tetsuya; Iki, Masami
PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

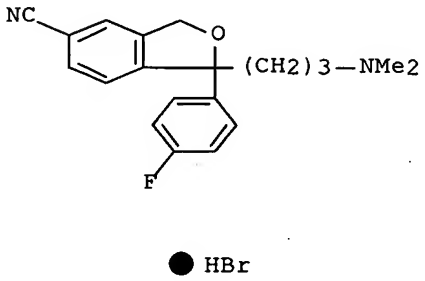
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003206284	A	20030722	JP 2001-401695	20011228 <--
PRIORITY APPLN. INFO.:			JP 2001-401695	20011228

AB Citalopram (I), useful as an antidepressant (no data), or its salts are prepared by treatment of the carbonitrile (II) with the chloride (III) in the presence of condensing agents and treatment of the reaction mixture with NaHSO3 in the presence of water to increase water solubility of byproducts and remove them. Alternatively, the reaction mixture is heated at ≥65° (after salt formation). Thus, II was condensed with III in the presence of NaH and aqueous NaHSO3 solution added to give 97% I with purity 92.88%.
IT 59729-33-8P, Citalopram
RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(purification of high-purity citalopram as antidepressant)
RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



IT 59729-32-7P, Citalopram hydrobromide
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(purification of high-purity citalopram as antidepressant)
RN 59729-32-7 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



L34 ANSWER 9 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:551309 CAPLUS Full-text
DOCUMENT NUMBER: 139:117333
TITLE: Process for the preparation of 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile via cyanation of the corresponding chloride or bromide precursors.
INVENTOR(S): Thennati, Rajamannar; Kilaru, Srinivasu; Chinnapillai, Rajendran; Patel, Nileshkumar Sureshbhai
PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Limited, India
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057132	A2	20030717	WO 2003-IN6	20030107 <--
WO 2003057132	A3	20040226		
WO 2003057132	A8	20040415		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

IN 193663	A1	20040731	IN 2002-MU10	20020107
IN 2002MU00847	A	20040703	IN 2002-MU847	20020930
AU 2003222435	A1	20030724	AU 2003-222435	20030107 <--
US 2005043550	A1	20050224	US 2004-500532	20040719
US 7148364	B2	20061212		

PRIORITY APPLN. INFO.:

IN 2002-MU10	A	20020107
IN 2002-MU18	A	20020110
IN 2002-MU847	A	20020930
WO 2003-IN6	W	20030107

OTHER SOURCE(S): CASREACT 139:117333; MARPAT 139:117333

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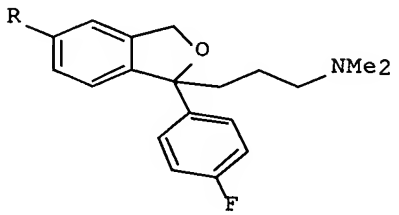


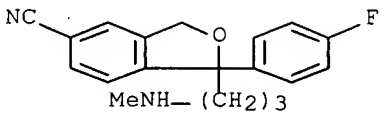
I

AB Title compound (I; R = cyano) (citalopram) was prepared by treatment of I (R = Cl, Br) with a cyanide source in the presence of I- in an amide, amine, or polyether solvent followed by treatment of the crude product containing 1-[3-(methylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile and 5-carboxamido-1-(3-dimethylaminopropyl)-1-(4-fluorophenyl)phthalide impurities with a phosphorus oxyhalide, phosphorus oxide cyanide reversal agent, and purification using a solvent system comprising a hydrocarbon and alc., ester, ether, ketone, or mixture thereof. Thus, citalopram containing 4.7% amide and 0.72% desmethylcitalopram impurities was heated with POCl3 in PhMe at 70° for 1 h. The mixture was poured into water and pH was adjusted to 2.0-2.5 with aqueous HCl. The PhMe layer was separated and the pH of the aqueous layer was adjusted to 9.0-9.5 with aqueous NH3 followed by extraction with PhMe to give product containing 0.05% and 0.23% of the amide and desmethylcitalopram resp.

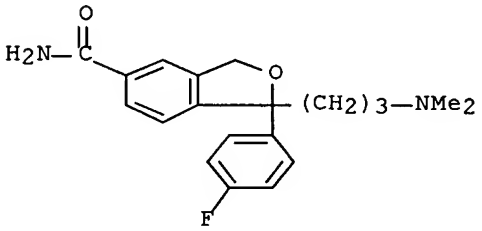
IT 62498-67-3P 64372-56-1P
RL: BYP (Byproduct); PREP (Preparation)
(process for the preparation of citalopram via cyanation of the corresponding chloride or bromide precursor)

RN 62498-67-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-(methylamino)propyl]- (CA INDEX NAME)

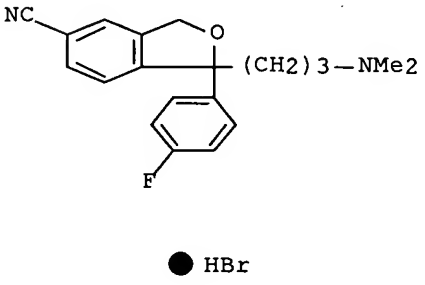


RN 64372-56-1 CAPLUS
CN 5-Isobenzofurancarboxamide, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

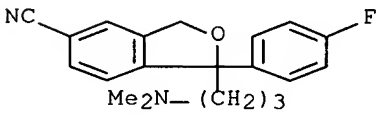


IT 59729-32-7P, Citalopram hydrobromide 59729-33-8P, 1-[3-(Dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for the preparation of citalopram via cyanation of the corresponding chloride or bromide precursor)

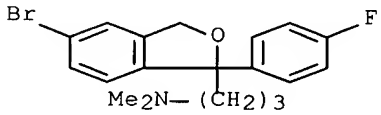
RN 59729-32-7 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



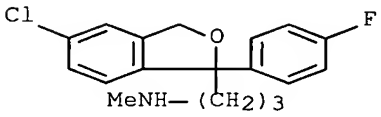
RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



IT 64169-39-7 561304-25-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the preparation of citalopram via cyanation of the corresponding chloride or bromide precursor)
RN 64169-39-7 CAPLUS
CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (CA INDEX NAME)



RN 561304-25-4 CAPLUS
CN 1-Isobenzofuranpropanamine, 5-chloro-1-(4-fluorophenyl)-1,3-dihydro-N-methyl- (9CI) (CA INDEX NAME)



L34 ANSWER 10 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:117613 CAPLUS Full-text
DOCUMENT NUMBER: 138:142518
TITLE: Crystalline composition containing escitalopram
INVENTOR(S): Christensen, Troels Volsgaard; Liljegren, Ken; Elema, Michiel Onne; Andresen, Lene; Mahashabde, Shashank; Assenza, Sebastian P.
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003011278	A1	20030213	WO 2002-DK513	20020725 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2451915	A1	20030213	CA 2002-2451915	20020725 <--
AU 2002355624	A1	20030217	AU 2002-355624	20020725 <--
BR 2002006164	A	20031028	BR 2002-6164	20020725 <--
EP 1414435	A1	20040506	EP 2002-750846	20020725
EP 1414435	B1	20050112		
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CN 1536997	A	20041013	CN 2002-815031	20020725
TR 200400189	T2	20041221	TR 2004-189	20020725
ZA 2003009684	A	20041222	ZA 2003-9684	20020725
AT 286730	T	20050115	AT 2002-750846	20020725
HU 200401946	A2	20050128	HU 2004-1946	20020725
EP 1522539	A1	20050413	EP 2004-29282	20020725
EP 1522539	B1	20070124		
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ES 2233842	T3	20050616	ES 2002-2750846	20020725
CN 1660074	A	20050831	CN 2004-10094166	20020725
JP 2005525993	T	20050902	JP 2003-516508	20020725
AT 352546	T	20070215	AT 2004-29282	20020725
NZ 530157	A	20070629	NZ 2002-530157	20020725
US 2003212128	A1	20031113	US 2003-403453	20030331 <--
US 6916941	B2	20050712		
MX 2004PA00849	A	20040514	MX 2004-PA849	20040127
BG 108571	A	20050228	BG 2004-108571	20040209
IN 2004CN00405	A	20051223	IN 2004-CN405	20040227
US 2005147674	A1	20050707	US 2005-53641	20050207

PRIORITY APPLN. INFO.:	DK 2001-1164	A 20010731
	DK 2001-164	A 20010731
	CN 2002-815031	A3 20020725
	EP 2002-750846	A3 20020725
	WO 2002-DK513	W 20020725
	US 2003-403453	A1 20030331

AB Crystalline particles of escitalopram oxalate with a particle size of at least 40 μm is disclosed. Method for the manufacture of the crystalline particles and pharmaceutical compns. comprising the crystalline particles are also disclosed. Thus, a tablet core was prepared from escitalopram oxalate 10.2, talc 5.6, Prosolv SMCC90 79.6, AcDiSol 3.6, and Mg stearate 1.0%. The film coating contained Opadry OY-S-28849 2.5% by weight Tablets were prepared from the above composition

IT 219861-08-2, Escitalopram oxalate
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(crystalline composition containing escitalopram)

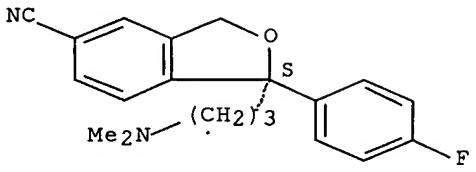
RN 219861-08-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1), (1S)- (CA INDEX NAME)

CM 1

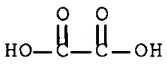
CRN 128196-01-0
CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (+).



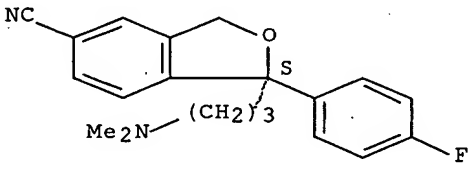
CM 2

CRN 144-62-7
CMF C2 H2 O4



IT 128196-01-0, Escitalopram
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crystalline composition containing escitalopram)
RN 128196-01-0 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 11 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:5943 CAPLUS Full-text
DOCUMENT NUMBER: 138:73169
TITLE: Preparation of racemic citalopram and/or S- or R-citalopram by separation of a mixture of R- and S-citalopram
INVENTOR(S): Humble, Rikke Eva; Christensen, Troels Volsgaard; Rock, Michael Harold; Nielsen, Ole; Petersen, Hans; Dancer, Robert
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000672	A1	20030103	WO 2002-DK426	20020625 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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CA 2450890	A1	20030103	CA 2002-2450890	20020625 <--
AU 2002344948	A1	20030108	AU 2002-344948	20020625 <--
AU 2002344948	B2	20070816		
EP 1412341	A1	20040428	EP 2002-742848	20020625
EP 1412341	B1	20041208		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002010574	A	20040803	BR 2002-10574	20020625
CN 1520405	A	20040811	CN 2002-812668	20020625
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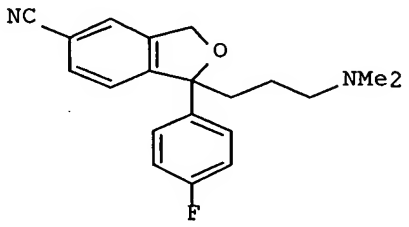
HU 200400293	A3	20070529		
JP 2004536093	T	20041202	JP 2003-507077	20020625
AT 284395	T	20041215	AT 2002-742848	20020625
PT 1412341	T	20050429	PT 2002-742848	20020625
ES 2233834	T3	20050616	ES 2002-2742848	20020625
TW 236473	B	20050721	TW 2002-91113845	20020625
NZ 530104	A	20060831	NZ 2002-530104	20020625
ZA 2003009633	A	20041213	ZA 2003-9633	20031211
MX 2003PA11770	A	20040402	MX 2003-PA11770	20031217
BG 108532	A	20050430	BG 2004-108532	20040114
IN 2004CN00142	A	20051209	IN 2004-CN142	20040123
US 2004259940	A1	20041223	US 2004-482000	20040209
US 7112686	B2	20060926		

PRIORITY APPLN. INFO.: DK 2001-991 A 20010625
WO 2002-DK426 W 20020625

OTHER SOURCE(S): CASREACT 138:73169

GI



I

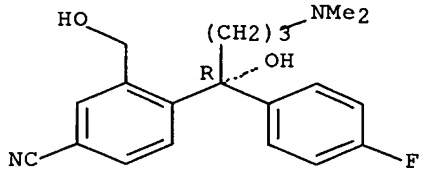
AB Citalopram (I), free base or an acid addition salt thereof, and/or R- or S-citalopram as the free base or an acid addition salt thereof, were prepared by separation of a mixture of R- and S-citalopram with more than 50% of one of the enantiomers into a fraction consisting of racemic citalopram and/or a fraction of S-citalopram or R-citalopram. The mixture of R- and S-citalopram was generally prepared by acid- or base-catalyzed ring closure of R- or S-[4-

(dimethylamino)-1-(4'- fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile. Racemic citalopram and S-citalopram are well-known antidepressants (no data).

IT 481047-48-7 488787-59-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(acid- or base-catalyzed ring closure of; preparation of citalopram)

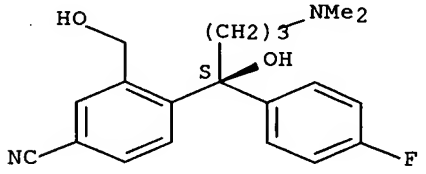
RN 481047-48-7 CAPLUS
CN Benzonitrile, 4-[(1R)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 488787-59-3 CAPLUS
CN Benzonitrile, 4-[(1S)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)

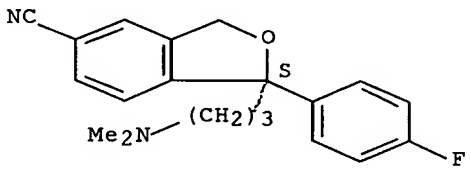
Absolute stereochemistry. Rotation (-).



IT 128196-01-0P, (S)-Citalopram 128196-02-1P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of citalopram)

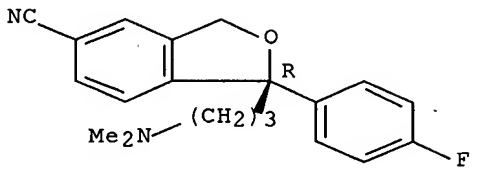
RN 128196-01-0 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



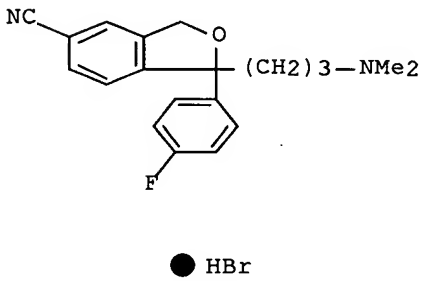
RN 128196-02-1 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

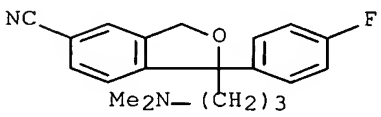


IT 59729-32-7P 59729-33-8P, Citalopram 219861-08-2P
219861-53-7P 481047-49-8P, (R)-Citalopram hydrobromide
481047-50-1P, (S)-Citalopram hydrobromide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of citalopram)

RN 59729-32-7 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)

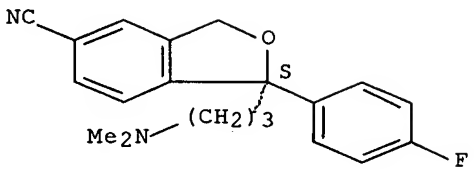


RN 219861-08-2 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1), (1S)- (CA INDEX NAME)

CM 1

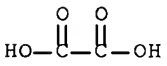
CRN 128196-01-0
CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (+).



CM 2

CRN 144-62-7
CMF C2 H2 O4

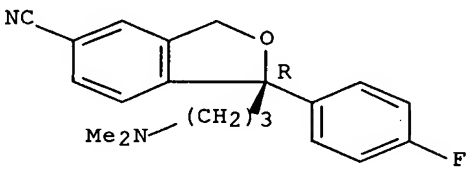


RN 219861-53-7 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1R)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

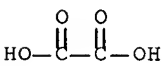
CRN 128196-02-1
CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (-).



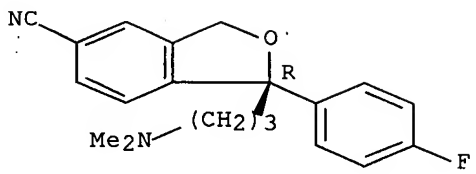
CM 2

CRN 144-62-7
CMF C2 H2 O4



RN 481047-49-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide, (1R)- (9CI) (CA INDEX NAME)

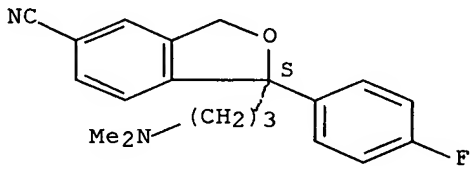
Absolute stereochemistry. Rotation (-).



● HBr

RN 481047-50-1 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1), (1S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HBr

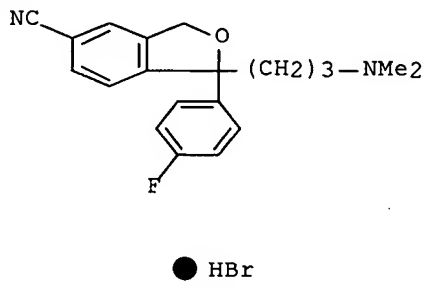
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 12 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:975673 CAPLUS Full-text
DOCUMENT NUMBER: 138:24637
TITLE: Preparation of citalopram hydrobromide
INVENTOR(S): Arai, Nobuhiro; Ikemoto, Tetsuya; Iki, Masami
PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

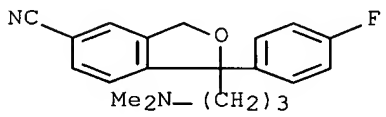
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002371077	A	20021226	JP 2001-174531	20010608 <--

PRIORITY APPLN. INFO.: JP 2001-174531 20010608
OTHER SOURCE(S): CASREACT 138:24637
AB The title antidepressant is prepared by treating citalopram with HBr in acetone followed by crystallization in the presence of citalopram hydrobromide seed crystals. Thus, citalopram was dissolved in acetone, treated with HBr, crystallized in the presence citalopram hydrobromide seed crystals to give 74.8% citalopram hydrobromide.
IT 59729-32-7P, Citalopram hydrobromide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of citalopram hydrobromide)

RN 59729-32-7 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



IT 59729-33-8, Citalopram
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of citalopram hydrobromide)
RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



L34 ANSWER 13 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:849904 CAPLUS Full-text
DOCUMENT NUMBER: 137:332583
TITLE: Hollow fiber membrane sample preparation devices
INVENTOR(S): Kallury, Krishna; Fan, Joy; Rasmussen, Knut; Pedersen-Bjergaard, Stig
PATENT ASSIGNEE(S): Varian, Inc., USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002088672	A1	20021107	WO 2002-US12952	20020425 <--
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2445316	A1	20021107	CA 2002-2445316	20020425 <--
AU 2002307529	A1	20021111	AU 2002-307529	20020425 <--
AU 2002307529	B2	20070201		
EP 1388005	A1	20040211	EP 2002-766799	20020425
EP 1388005	B1	20061115		

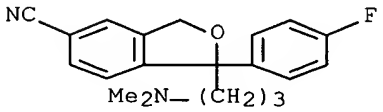
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004535563	T	20041125	JP 2002-585927	20020425
US 2004171169	A1	20040902	US 2004-475896	20040406
PRIORITY APPLN. INFO.:			US 2001-287158P	P 20010426
			WO 2002-US12952	W 20020425

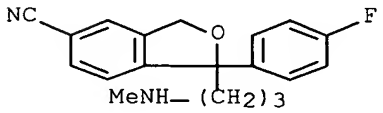
AB Simultaneous sample purification, enrichment and anal. of pharmaceuticals, illicit drugs, pollutants, biotechnol. products, synthetic organic reaction products and food/flavor ingredients from complex matrixes can be performed using porous hollow fiber or porous-disk liquid-membrane devices. The devices are part of a multi-well (e.g. 96-well) plate. The devices can be used for selective separation and enrichment of complex mixts. containing trace levels of analytes, and can be used in tandem with anal. instruments which routinely handle multiple samples under high throughput screening conditions. A multi-well/multi-vial plate can into state-of-the-art HPLC or GC sampling systems or LC/MS or GC/MS instruments. Samples can be enriched several orders of magnitude and can directly be withdrawn from the fiber and injected into the chromatog. instruments. Alternatively, these enriched samples can be introduced directly into MS, CE or other detection devices. Selective extraction of complex mixts. of analytes can be achieved through variation of acceptor phase chemical, liquid membrane coating, pore size control of the hollow fibers, nature of the polymer from which the hollow fibers are made or pH of the acceptor phase.

IT 59729-33-8, Citalopram 62498-67-3, Desmethyl citalopram
RL: ANT (Analyte); ANST (Analytical study)
(separation and enrichment of pharmaceuticals from body fluids with hollow fiber membrane sample preparation system)

RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



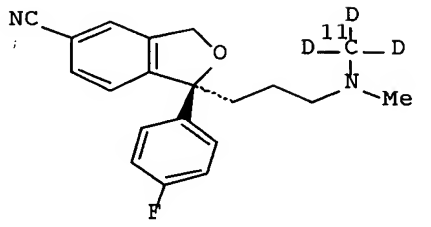
RN 62498-67-3 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-(methylamino)propyl]- (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 14 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:174806 CAPLUS Full-text
DOCUMENT NUMBER: 137:369908
TITLE: Gas phase production of 11CD3I and synthesis of S-[N-D3-methyl-11C]citalopram

AUTHOR(S): Madsen, Jacob; Andersen, Kim; Knudsen, Gitte M.; Martiny, Lars
CORPORATE SOURCE: PET & Cyclotron Unit, Copenhagen University Hospital, Copenhagen, DK-2100, Den.
SOURCE: Synthesis and Applications of Isotopically Labelled Compounds, Proceedings of the International Symposium, 7th, Dresden, Germany, June 18-22, 2000 (2001***) , Meeting Date 2000, 347-350. Editor(s): Pleiss, Ulrich; Voges, Rolf. John Wiley & Sons Ltd.: Chichester, UK.
CODEN: 69CIJC; ISBN: 0-471-49501-8
DOCUMENT TYPE: Conference
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:369908
GI



I

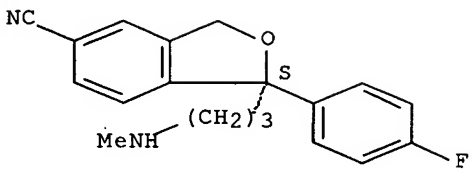
AB The preparation of 11CH3I in a gas phase reaction was expanded to include the formation of 11CD3I. Bombarding a mixture of N2 and D2 with 16 MeV protons in a gas target and trapped on a porapak N column at -190° yielded 11CD4. After warmup, the 11CD4 and I2 vapors were in several cycles passed through a quartz tube at 720 °. At the end of each reaction cycle 11CD3I was trapped on the Porapak N column at room temperature At the point when reacted 11CD4 was recirculated through the quartz tube, the 11CD3I was liberated by purging the Porapak trap at 190 ° with helium. S-N-Desmethyl-citalopram monofumarate was methylated in ethanol and 1,2,2,6,6-pentamethyl-piperidine (PMP) at reflux temperature producing S-[N-d3-methyl11C]citalopram I. After purification the radiochem. purity was > 99% and the radiochem. yield in the labeling step was 34%. The specific activity of the final product obtained was 0.65 Ci/μmol EOS with a 45 min total synthesis time. A higher specific activity (2.5-3.5 Ci/μmol EOS) of S-[N-methyl-11C]-citalopram was achieved when 11 CH3I was yielded with N2/H2 (95%/5%) as the target gas.

IT 144025-14-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of isotopically labeled S-[N-D3-methyl-11C]citalopram via methylation of corresponding N-methylamine with 11CD3I)

RN 144025-14-9 CAPLUS

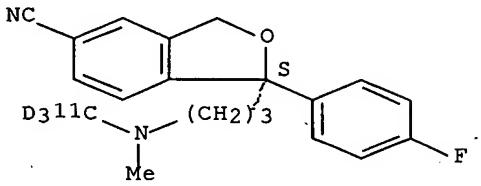
CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-(methylamino)propyl]-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 475107-77-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of isotopically labeled S-[N-D3-methyl-11C]citalopram via methylation of corresponding N-methylamine with 11CD3I)
RN 475107-77-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-(methylmethyl-11C-d3-amino)propyl]-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

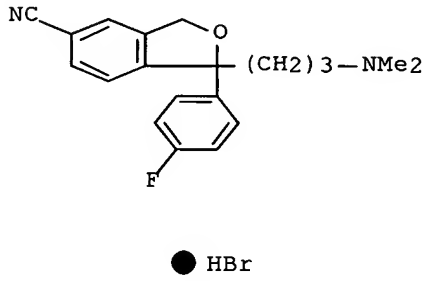
L34 ANSWER 15 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:814053 CAPLUS Full-text
DOCUMENT NUMBER: 135:348923
TITLE: Citalopram hydrobromide crystals and crystallization
INVENTOR(S): Ikemoto, Tetsuya; Arai, Nobuhiro; Igi, Masami
PATENT ASSIGNEE(S): Sumika Fine Chemicals Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 31 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1152000	A1	20011107	EP 2001-108914	20010410 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002020379	A	20020123	JP 2001-102717	20010330 <--
US 2001049450	A1	20011206	US 2001-824447	20010402 <--
US 6977306	B2	20051220		
CA 2343543	A1	20011102	CA 2001-2343543	20010409 <--
AU 782717	B2	20050825	AU 2001-35085	20010410
PRIORITY APPLN. INFO.:			JP 2000-133995 A	20000502

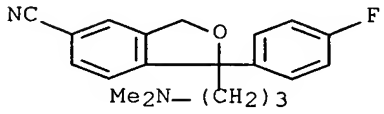
AB Citalopram-HBr is dissolved in a solvent containing at least one member selected from the group consisting of alc. having 1-3 carbon atoms, water and acetone is crystallized or recrystd. while controlling the cooling rate,

thereby to 1) provide an industrial method for crystallizing citalopram-HBr, which enables easy control of the crystal characteristics, such as particle size, particle size distribution and aspect ratio and the like of the crystal, and 2) provide citalopram-HBr crystal having crystal characteristics useful as a pharmaceutical bulk.

IT 59729-32-7P, Citalopram hydrobromide
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(citalopram hydrobromide crystals and crystallization)
RN 59729-32-7 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



IT 59729-33-8, Citalopram
RL: RCT (Reactant); RACT (Reactant or reagent)
(citalopram hydrobromide crystals and crystallization)
RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 16 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:797983 CAPLUS Full-text
DOCUMENT NUMBER: 135:348880
TITLE: Pharmaceutical composition containing citalopram
INVENTOR(S): Liljegren, Ken; Holm, Per; Nielsen, Ole; Wagner, Sven
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

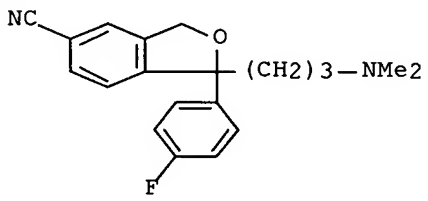
WO 2001080619	A2	20011101	WO 2001-DK520	20010730 <--	
WO 2001080619	A3	20020221			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2353693	A1	20020122	CA 2001-2353693	20010724 <--	
CA 2353693	C	20030722			
AU 2001100198	A4	20010816	AU 2001-100198	20010726 <--	
AU 2001100198	B4	20020613			
HU 200103071	A2	20020529	HU 2001-3071	20010726 <--	
AU 200179591	A	20011107	AU 2001-79591	20010730 <--	
EP 1318805	A2	20030618	EP 2001-957768	20010730 <--	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001013250	A	20030624	BR 2001-13250	20010730 <--	
JP 2003531153	T	20031021	JP 2001-577732	20010730 <--	
NZ 523785	A	20040924	NZ 2001-523785	20010730	
GB 2368014	A	20020424	GB 2001-18579	20010731 <--	
GB 2368014	B	20040623			
GR 2001100377	A	20020906	GR 2001-100377	20010731 <--	
GR 1004193	B2	20030324			
GB 2376233	A	20021211	GB 2002-19820	20010731 <--	
GB 2376233	B	20030910			
FR 2812811	A1	20020215	FR 2001-10586	20010808 <--	
FR 2812811	B1	20060818			
CH 694242	A5	20041015	CH 2001-1469	20010808	
CH 694241	A5	20041015	CH 2003-1422	20010808	
DE 20113195	U1	20011220	DE 2001-20113195	20010809 <--	
NO 2001003891	A	20020211	NO 2001-3891	20010809 <--	
DE 10139115	A1	20020328	DE 2001-10139115	20010809 <--	
ES 2172481	A1	20020916	ES 2001-1877	20010809 <--	
ES 2172481	B2	20040801			
NL 1018741	C1	20020212	NL 2001-1018741	20010810 <--	
BE 1013559	A6	20020305	BE 2001-537	20010810 <--	
ZA 2003000561	A	20040122	ZA 2003-561	20030121	
MX 2003PA00837	A	20030606	MX 2003-PA837	20030128 <--	
BG 107578	A	20030930	BG 2003-107578	20030221 <--	
PRIORITY APPLN. INFO.:			DK 2000-1202	A 20000810	
			DK 2000-1614	A 20001027	
			WO 2001-DK520	W 20010730	
			GB 2001-18579	A3 20010731	

AB A solid unit dosage form comprises citalopram, which is prepared by direct compression of a mixture of citalopram base or a salt and excipients, or by filling of the mixture in a hard gelatin capsule. Large crystals of a pharmaceutical salt of citalopram and method for the manufacture of large crystals are also disclosed. Thus, citalopram-HBr was dissolved in a mixture of MeOH and water at 69°, the solution was cooled to 30°, seeded with the same drug crystals and kept at 30° for 24 h, whereupon it was cooled down to 10° within 1 h. The crystals were separated by filtration, washed with cold MeOH and dried. Tablets contained citalopram-HBr 20, Prosolv SMCC-90 79.5, and Mg stearate 0.5%.

IT 59729-32-7, Citalopram hydrobromide 59729-33-8, Citalopram 85118-27-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition containing citalopram)

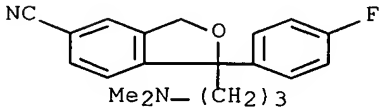
RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)

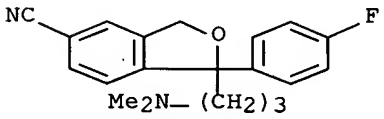


● HBr

RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



RN 85118-27-0 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

L34 ANSWER 17 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:489362 CAPLUS Full-text
DOCUMENT NUMBER: 135:61225
TITLE: Process for the preparation of high-purity citalopram by cyanidation with purification via thin-film distillation
INVENTOR(S): Castellin, Andrea; Volpe, Giulio; Sbrogio, Federico
PATENT ASSIGNEE(S): H. Lundbeck A/s, Den.
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047877	A2	20010705	WO 2001-DK148	20010307 <--
WO 2001047877	A3	20001227		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2359810	A1	20010705	CA 2001-2359810	20010307 <--
CA 2359810	C	20021105		
AU 200139202	A	20010709	AU 2001-39202	20010307 <--
AU 2001100399	A4	20011101	AU 2001-100399	20010307 <--
AU 2001100399	B4	20020321		
EP 1181272	A2	20020227	EP 2001-913727	20010307 <--
EP 1181272	B1	20020828		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2001006271	A	20020521	BR 2001-6271	20010307 <--
TR 200200018	T1	20020621	TR 2002-18	20010307 <--
AT 222899	T	20020915	AT 2001-913727	20010307 <--
PT 1181272	T	20030131	PT 2001-913727	20010307 <--
ES 2181663	T3	20030301	ES 2001-1913727	20010307 <--
JP 2003519121	T	20030617	JP 2001-549350	20010307 <--
SK 284418	B6	20050401	SK 2001-1847	20010307
NL 1017534	C1	20010426	NL 2001-1017534	20010308 <--
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OTHER SOURCE(S): CASREACT 135:61225; MARPAT 135:61225

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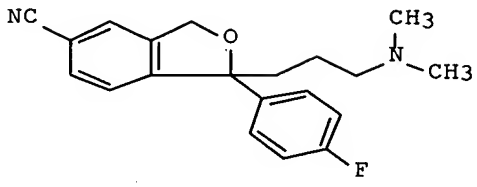

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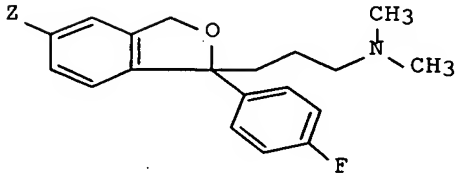


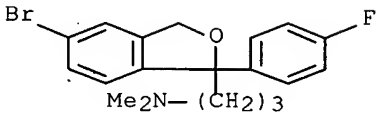
II

AB High-purity citalopram (I) is prepared on an industrial scale by: subjecting a citalopram precursor [II; Z = iodo, bromo, chloro, CF3(CF2)nSO2O; n = 0-8] (e.g., Z = Br) to a cyanide exchange reaction in which the group Z is exchanged with cyanide by reaction with a cyanide source (e.g., CuCN) in a solvent (e.g., sulfolane); the crude citalopram product is optionally subjected to some initial purification and the crude citalopram base is subsequently subjected to a thin- or falling-film distillation process.

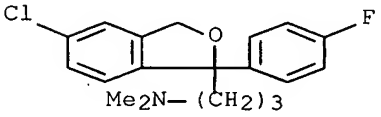
IT 64169-39-7 64169-45-5 260066-78-2
260066-82-8 345658-19-7 345658-20-0
345658-21-1 345658-22-2 345658-23-3
345658-24-4 345658-25-5 345658-26-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(in a process for the preparation of high-purity citalopram by cyanidation with purification via thin-film distillation)

RN 64169-39-7 CAPLUS

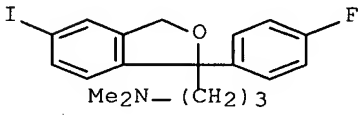
CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (CA INDEX NAME)



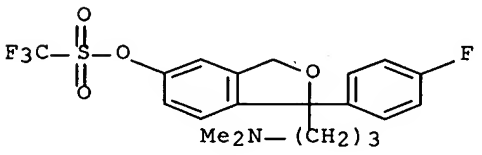
RN 64169-45-5 CAPLUS
CN 1-Isobenzofuranpropanamine, 5-chloro-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)



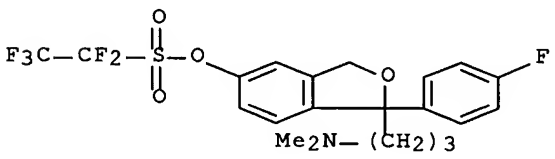
RN 260066-78-2 CAPLUS
CN 1-Isobenzofuranpropanamine, 1-(4-fluorophenyl)-1,3-dihydro-5-iodo-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 260066-82-8 CAPLUS
CN Methanesulfonic acid, trifluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)

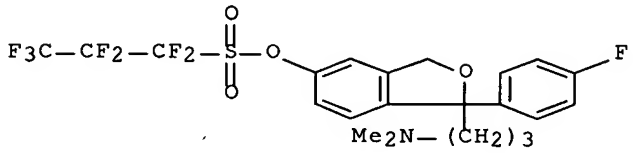


RN 345658-19-7 CAPLUS
CN Ethanesulfonic acid, pentafluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)



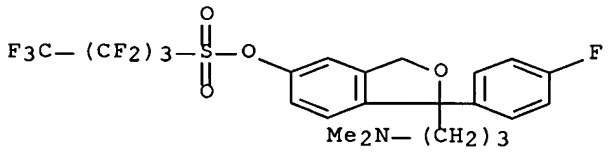
RN 345658-20-0 CAPLUS

CN 1-Propanesulfonic acid, 1,1,2,2,3,3,3-heptafluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)



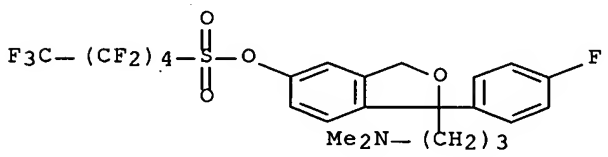
RN 345658-21-1 CAPLUS

CN 1-Butanesulfonic acid, 1,1,2,2,3,3,4,4,4-nonafluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)



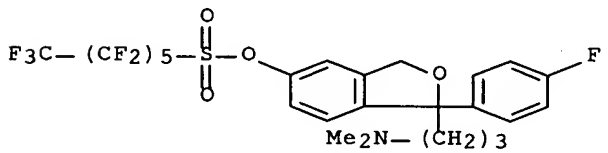
RN 345658-22-2 CAPLUS

CN 1-Pentanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,5-undecafluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)



RN 345658-23-3 CAPLUS

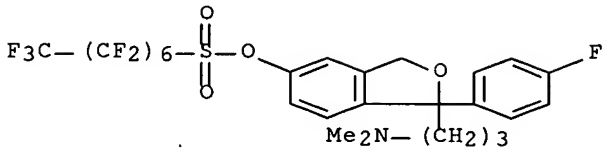
CN 1-Hexanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)



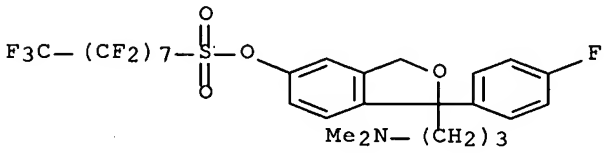
RN 345658-24-4 CAPLUS

CN 1-Heptanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,7-pentadecafluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-

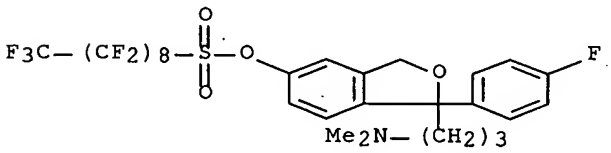
isobenzofuranyl ester (9CI) (CA INDEX NAME)



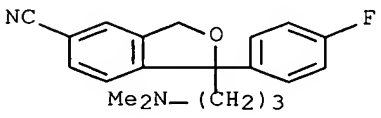
RN 345658-25-5 CAPLUS
CN 1-Octanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)



RN 345658-26-6 CAPLUS
CN 1-Nonanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-nonadecafluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)



IT 59729-33-8P, Citalopram
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for the preparation of high-purity citalopram by cyanidation with purification via thin-film distillation)
RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



L34 ANSWER 18 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:472398 CAPLUS Full-text

DOCUMENT NUMBER: 135:61224
TITLE: Method for the preparation and purification of citalopram
INVENTOR(S): Villa, Marcos; Sbrogio, Federico; Dancer, Robert
PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001045483	A2	20010628	WO 2001-DK147	20010307 <--
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OTHER SOURCE(S): CASREACT 135:61224; MARPAT 135:61224

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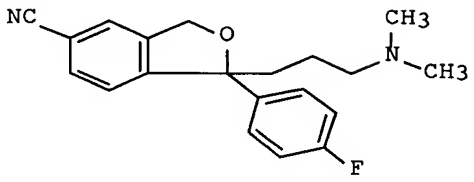

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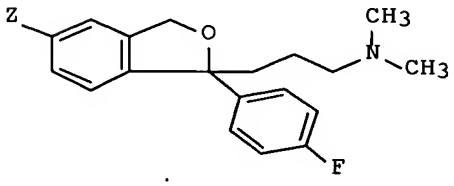


II

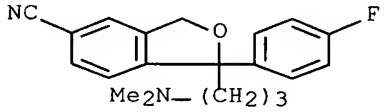
AB A process for the preparation and purification of citalopram (I) is presented in which a benzoisofuran derivative [II; Z = iodo, bromo, chloro, CF3(CF2)nSO2O; n = 0-8] is subjected to a cyanide-exchange reaction with a cyanide source (e.g., cuprous cyanide). The resultant crude citalopram is optionally subjected to some initial purification and subsequently treated with an amide or an amide-like group forming agent (e.g., acetic anhydride), the reaction mixture is then subjected to an acid/base wash and/or crystallization and recrystn. of citalopram in order to remove the amides formed from the crude citalopram mixture, and the resulting citalopram product is optionally further purified, worked up and isolated as the base or a pharmaceutically acceptable salt.

IT 59729-33-8P, Citalopram
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

(method for the preparation and purification of citalopram)

RN 59729-33-8 CAPLUS

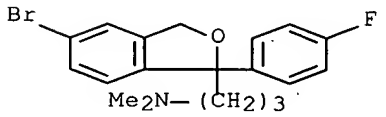
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



IT 64169-39-7 64169-45-5 260066-78-2
260066-82-8 345658-19-7 345658-20-0
345658-21-1 345658-22-2 345658-23-3
345658-24-4 345658-25-5 345658-26-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(method for the preparation of citalopram by the cyanidation of)

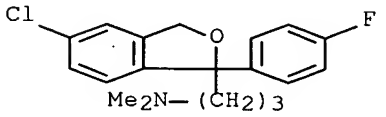
RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (CA INDEX NAME)



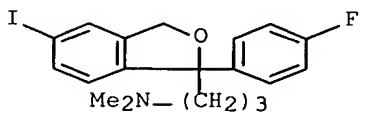
RN 64169-45-5 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-chloro-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 260066-78-2 CAPLUS

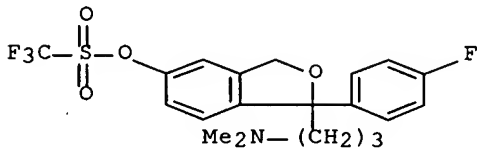
CN 1-Isobenzofuranpropanamine, 1-(4-fluorophenyl)-1,3-dihydro-5-iodo-N,N-dimethyl- (9CI) (CA INDEX NAME)



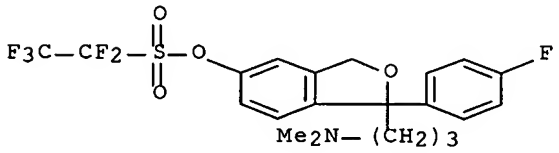
RN 260066-82-8 CAPLUS

CN Methanesulfonic acid, trifluoro-, 1-[3-(dimethylamino)propyl]-1-(4-

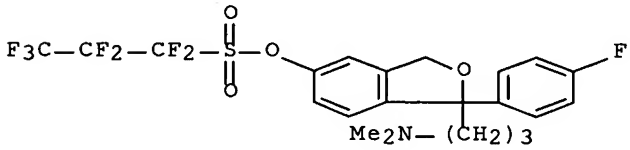
fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)



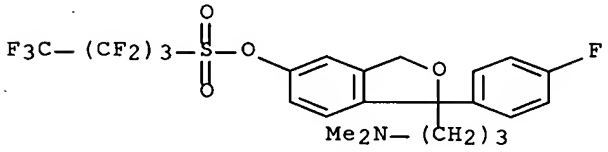
RN 345658-19-7 CAPLUS
CN Ethanesulfonic acid, pentafluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)



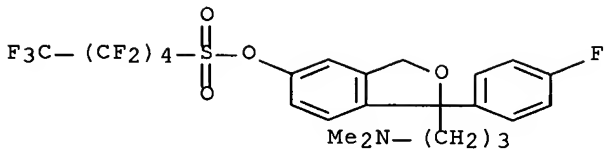
RN 345658-20-0 CAPLUS
CN 1-Propanesulfonic acid, 1,1,2,2,3,3,3-heptafluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)



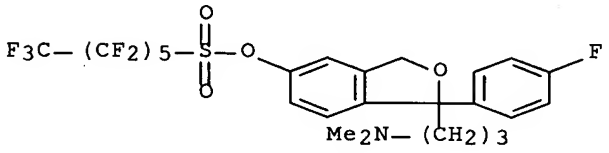
RN 345658-21-1 CAPLUS
CN 1-Butanesulfonic acid, 1,1,2,2,3,3,4,4,4-nonafluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)



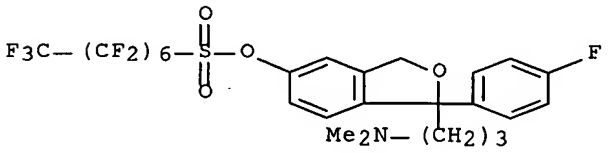
RN 345658-22-2 CAPLUS
CN 1-Pentanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,5-undecafluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)



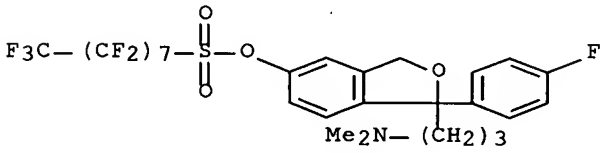
RN 345658-23-3 CAPLUS
CN 1-Hexanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,6-tridecafluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)



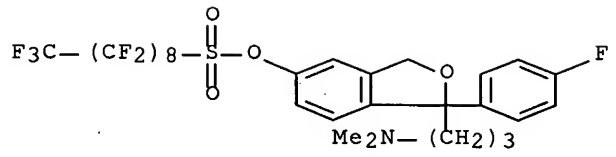
RN 345658-24-4 CAPLUS
CN 1-Heptanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,7-pentadecafluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)



RN 345658-25-5 CAPLUS
CN 1-Octanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)



RN 345658-26-6 CAPLUS
CN 1-Nonanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-nonadecafluoro-, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuranyl ester (9CI) (CA INDEX NAME)



L34 ANSWER 19 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:338762 CAPLUS Full-text
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103 <--
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105
US 2000-196571P P 20000411

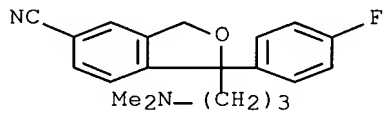
AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

IT 59729-33-8, Citalopram
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



L34 ANSWER 20 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:607941 CAPLUS Full-text

DOCUMENT NUMBER: 133:213148

TITLE: Crystalline base of citalopram

PATENT ASSIGNEE(S): H. Lundbeck A/S, Den.

SOURCE: Ger. Gebrauchsmusterschrift, 17 pp.
CODEN: GGXXFR

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 20007303	U1	20000831	DE 2000-20007303	20000420 <--
GB 2357762	A	20010704	GB 2001-5982	20000413 <--
GB 2357762	B	20020130		
NL 1016435	C1	20001106	NL 2000-1016435	20001018 <--
IT 2000MI2425	A1	20020509	IT 2000-MI2425	20001109 <--
IT 1319645	B1	20031023		
US 2001031784	A1	20011018	US 2000-730490	20001205 <--
IN 2001MA00091	A	20050304	IN 2001-MA91	20010201
HU 200100531	A2	20020128	HU 2001-531	20010205 <--
DK 173903	B1	20020211	DK 2001-183	20010205 <--
HU 200400868	A3	20070529	HU 2004-868	20010205
NO 2001000619	A	20010914	NO 2001-619	20010206 <--
NO 312031	B1	20020304		
FI 2001000225	A	20010914	FI 2001-225	20010207 <--
FI 109022	B1	20020515		
GR 1003796	B2	20020208	GR 2001-100074	20010212 <--
DE 10108042	A1	20011018	DE 2001-10108042	20010220 <--
DE 20121240	U1	20020808	DE 2001-20121240	20010220 <--
DE 10164687	B4	20060427	DE 2001-10164687	20010220
NL 1017413	C1	20010913	NL 2001-1017413	20010221 <--
FR 2806086	A1	20010914	FR 2001-2340	20010221 <--
FR 2806086	B1	20030509		
CH 691477	A5	20010731	CH 2001-321	20010222 <--
CH 691537	A5	20010815	CH 2001-580	20010222 <--
AU 200137252	A	20010913	AU 2001-37252	20010228 <--
AU 746664	B2	20020502		
CA 2360287	A1	20010920	CA 2001-2360287	20010228 <--
CA 2360287	C	20030909		
CA 2411732	A1	20010920	CA 2001-2411732	20010228 <--
WO 2001068627	A1	20010920	WO 2001-DK137	20010228 <--

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CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

BE 1013210	A3	20011002	BE 2001-136	20010228	<--
EP 1169314	A1	20020109	EP 2001-909568	20010228	<--
EP 1169314	B1	20020904			

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IE, SI, LT, LV, FI, RO

EP 1227088	A1	20020731	EP 2002-9350	20010228	<--
EP 1227088	B1	20030917			

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IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

AT 223396	T	20020915	AT 2001-909568	20010228	<--
PT 1169314	T	20021129	PT 2001-909568	20010228	<--
ES 2173054	T3	20021216	ES 2001-1909568	20010228	<--
TR 200202185	T2	20021223	TR 2002-2185	20010228	<--
BR 2001009373	A	20021224	BR 2001-9373	20010228	<--
JP 2003527383	T	20030916	JP 2001-567719	20010228	<--
AT 250050	T	20031015	AT 2002-9350	20010228	<--
PT 1227088	T	20031231	PT 2002-9350	20010228	
ES 2180471	T3	20040501	ES 2002-2009350	20010228	
CN 1680350	A	20051012	CN 2005-10009160	20010228	
SK 285528	B6	20070301	SK 2002-1313	20010228	
CZ 292077	B6	20030716	CZ 2001-808	20010305	<--
IN 193191	A1	20040710	IN 2001-MA209	20010308	
ES 2159491	A1	20011001	ES 2001-548	20010309	<--
ES 2159491	B1	20020501			
AU 2001100197	A4	20010920	AU 2001-100197	20010726	<--
AU 2001100197	B4	20011206			
SE 2001003046	A	20011114	SE 2001-3046	20010914	<--
SE 517136	C2	20020416			
NO 2002000356	A	20010914	NO 2002-356	20020123	<--
NO 315851	B1	20031103			
SE 2002000730	A	20020829	SE 2002-730	20020312	<--
SE 526022	C2	20050614			
ZA 2002007148	A	20030423	ZA 2002-7148	20020905	<--
BG 107065	A	20030530	BG 2002-107065	20020905	<--
MX 2002PA08793	A	20030212	MX 2002-PA8793	20020909	<--
US 2003078442	A1	20030424	US 2002-245824	20020912	<--
IN 2002MA00828	A	20050304	IN 2002-MA828	20021111	
HK 1054750	A1	20070119	HK 2003-107120	20031002	
US 2004132808	A1	20040708	US 2003-741553	20031219	
US 2004167210	A1	20040826	US 2003-750049	20031230	
US 2005165092	A1	20050728	US 2005-90336	20050324	
US 2005165244	A1	20050728	US 2005-90337	20050324	
US 2006229459	A1	20061012	US 2006-425308	20060620	
US 2006247451	A1	20061102	US 2006-425321	20060620	

PRIORITY APPLN. INFO.:

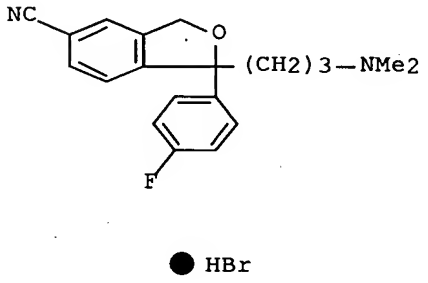
DK 2000-402	A	20000313
WO 2000-DK183	W	20000413
DE 2000-10019609	A1	20000420
DK 2001-183	A	20010205
DE 2001-10108042	IA	20010220
AU 2001-37252	A3	20010228
CN 2001-809341	A3	20010228
EP 2001-909568	A3	20010228

WO 2001-DK137	W	20010228
US 2002-245824	A1	20020912
CA 2003-2360287	A3	20030113
US 2003-741553	B1	20031219
US 2003-750049	B1	20031230
US 2005-90336	A1	20050324
US 2005-90337	B1	20050324

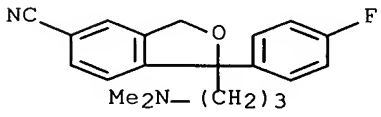
AB Citalopram, a selective, centrally acting serotonin reuptake inhibitor useful as an antidepressant, is prepared in high purity from a crude salt or reaction mixture containing citalopram by dissolving the latter in a mixture of H2O and an organic solvent, adding a base, separating and evaporating the organic phase, and crystallization from an aprotic solvent. The free base may then be converted to a salt by reaction with the stoichiometric amount of an acid (e.g. HCl, HBr) in a water-miscible solvent (e.g. Me2CO, EtOH), concentration, and cooling, or by reaction with an excess of acid in Et2O, EtOAc, or CH2Cl2 for formulation as tablets, capsules, powders, syrups, or solns. for injection.

IT 59729-32-7P, Citalopram hydrobromide 59729-33-8P, Citalopram 85118-27-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystalline base of citalopram)

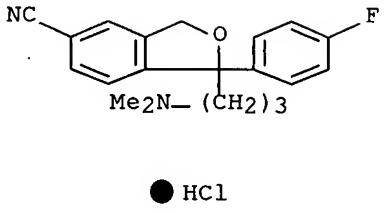
RN 59729-32-7 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



RN 85118-27-0 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrochloride (1:1) (CA INDEX NAME)



L34 ANSWER 21 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:204419 CAPLUS Full-text
DOCUMENT NUMBER: 128:261968
TITLE: Pharmaceutical composition containing combination of atypical antipsychotic and serotonin reuptake inhibitor for treatment of psychoses
INVENTOR(S): Bymaster, Franklin Porter; Perry, Kenneth Wayne; Tollefson, Gary Dennis
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 830864	A1	19980325	EP 1997-307375	19970922 <--
EP 830864	B1	20030129		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
ZA 9707967	A	19990304	ZA 1997-7967	19970904 <--
CA 2264941	A1	19980326	CA 1997-2264941	19970909 <--
WO 9811897	A1	19980326	WO 1997-US15874	19970909 <--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9744112	A	19980414	AU 1997-44112	19970909 <--
AU 719033	B2	20000504		
BR 9711530	A	19990824	BR 1997-11530	19970909 <--
CN 1230886	A	19991006	CN 1997-198113	19970909 <--
NZ 334168	A	20000929	NZ 1997-334168	19970909 <--
HU 9903905	A2	20001028	HU 1999-3905	19970909 <--
JP 2001503031	T	20010306	JP 1998-514717	19970909 <--
PL 190374	B1	20051230	PL 1997-332481	19970909
TW 541178	B	20030711	TW 1997-86113280	19970912 <--
EP 1256345	A1	20021113	EP 2002-16238	19970922 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO, AL				
AT 231724	T	20030215	AT 1997-307375	19970922 <--
ES 2191152	T3	20030901	ES 1997-307375	19970922 <--
US 6147072	A	20001114	US 1997-935872	19970923 <--
HK 1009755	A1	20031024	HK 1998-110801	19980921 <--
NO 9901381	A	19990322	NO 1999-1381	19990322 <--

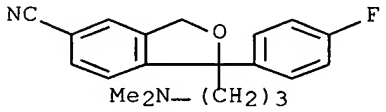
NO 319166	B1	20050627		
KR 2000048518	A	20000725	KR 1999-702422	19990322 <--
PRIORITY APPLN. INFO.:			US 1996-26884P	P 19960923
			WO 1997-US15874	W 19970909
			EP 1997-307375	A3 19970922

AB Pharmaceutical compns. containing combination of atypical antipsychotics and serotonin reuptake inhibitors are useful for the treatment of psychoses. Form II olanzapine (I) polymorph was prepared by heating I at 76° for 30 min in Et acetate and crystallization Hard gelatin capsules contained I 25, fluoxetin hydrochloride 20, starch 150, and magnesium stearate 10 mg.

IT 59729-33-8, Citalopram
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition containing combination of atypical antipsychotic and
serotonin reuptake inhibitor for treatment of psychoses)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 22 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1996:154442 CAPLUS Full-text
DOCUMENT NUMBER:	124:228035
TITLE:	The serotonin transporter from human brain: purification and partial characterization
AUTHOR(S):	Rotondo, A.; Giannaccini, G.; Betti, L.; Chiellini, G.; Marazziti, D.; Martin, C.; Lucacchini, A.; Cassano, G. B.
CORPORATE SOURCE:	Inst. Psychiatry, Univ. Pisa, Pisa, 56100, Italy
SOURCE:	Neurochemistry International (1996), 28(3), 299-307 CODEN: NEUIDS; ISSN: 0197-0186
PUBLISHER:	Elsevier
DOCUMENT TYPE:	Journal
LANGUAGE:	English

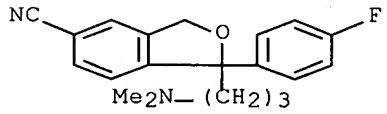
AB The serotonin (5-HT) transporter from human striatum was solubilized by digitonin and purified by affinity chromatog. The native protein-detergent complex had a mol. mass of 205 kDa, as estimated by gel-exclusion chromatog. of the eluates obtained from affinity chromatog. The purified 5-HT transporter migrated as a single band of 67 kDa in SDS-PAGE. To clarify the spatial relationships between the binding sites of the tricyclic antidepressants, as [3H]-imipramine, and of the selective serotonin reuptake inhibitors, such as [3H]-paroxetine, on the 5-HT transporter, both radioligands were used to label it in the purification steps. [3H]-paroxetine bound with the same affinity to a single high-affinity site on both membrane and purified prepns. [3H]-imipramine labeled a high- and a low-affinity site on parent membranes, whereas it bound to a single high-affinity site on the purified extract Tricyclic antidepressants, selective serotonin reuptake inhibitors and 5-HT

itself displaced [3H]-paroxetine 5-HT transporter in a monophasic fashion with Hill coeffs. close to unity. Furthermore, both [3H]-paroxetine and [3H]-imipramine displayed a similar maximum binding capacity on an identical protein of 205 kDa. The results suggest overlapping binding sites for tricyclic antidepressants, selective serotonin reuptake inhibitors and 5-HT on the 5-HT transporter.

IT 59729-33-8, Citalopram
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(purification and partial characterization of the serotonin transporter from human brain)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



L34 ANSWER 23 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:655736 CAPLUS Full-text

DOCUMENT NUMBER: 123:101882

TITLE: Simultaneous determination of citalopram and its metabolites by high-performance liquid chromatography with column switching and fluorescence detection by direct plasma injection

AUTHOR(S): Matsui, Eiji; Hoshino, Masanori; Matsui, Akiko; Okahira, Akira

CORPORATE SOURCE: Central Research Laboratories, Zeria Pharmaceutical Co., Ltd., 2512-1 Oshikiri, Konan-machi, Osato-gun, Saitama, 360-01, Japan

SOURCE: Journal of Chromatography, B: Biomedical Applications (1995), 668(2), 299-307
CODEN: JCBBEP; ISSN: 0378-4347

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

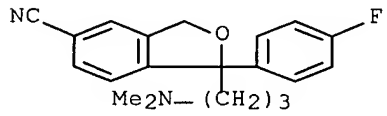
LANGUAGE: English

AB HPLC with a successive column-switching technique was developed for simultaneous determination of citalopram and its 4 metabolites in plasma. Plasma samples were injected directly, and the target compds. were purified and concentrated on an inexpensive com. octadecyl guard column. A 6-port valve was then opened, and the compds. retained in the column were eluted by the back-flush method, using 20 mM phosphate buffer (pH 4.6)-MeCN (70:30) containing 0.1% Et2NH, and separated with an ODS column. The compds. were assayed with a fluorescence detector at an excitation wavelength of 249 nm and an emission wavelength of 302 nm. At least 30 plasma samples could be treated with the octadecyl guard column before its exhaustion. The limits of quantitation of this method were 2.0 ng/mL for citalopram, demethylcitalopram, didemethylcitalopram, citalopram propionic acid and citalopram N-oxide. This method was applied to a pharmacokinetic study in dogs and a toxicokinetic study in rats.

IT 59729-33-8, Citalopram
RL: ANT (Analyte); ANST (Analytical study)
(determination of citalopram and its metabolites in plasma by HPLC)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



L34 ANSWER 24 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:608184 CAPLUS Full-text
DOCUMENT NUMBER: 117:208184
TITLE: Partial purification and characterization of the sodium-ion-coupled 5-hydroxytryptamine transporter of rat cerebral cortex
AUTHOR(S): Graham, David; Esnaud, Huguette; Langer, Salomon Z.
CORPORATE SOURCE: Synthelabo Rech., Bagneux, F-92220, Fr.
SOURCE: Biochemical Journal (1992), 286(3), 801-5
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English

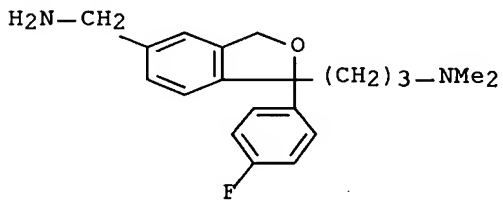
AB A procedure for the extensive purification of the Na+-coupled 5-hydroxytryptamine transporter of rat cerebral cortex was developed. The 5-hydroxytryptamine transporter was solubilized with the nonionic detergent digitonin, and the detergent exts. were subjected to sequential affinity chromatog. on a citalopram-based agarose support and wheat-germ-agglutinin-Sepharose. 5-Hydroxytryptamine transporters in the affinity-purified preparation were identified by using the selective 5-hydroxytryptamine-uptake inhibitor [3H]paroxetine, and were shown to display a similar pharmacol. profile to those present in particulate prepns. An overall transporter purification of around 2000-fold was achieved with a 9% recovery. SDS/PAGE of affinity-chromatographed material starting from detergent exts. incubated in the presence or absence of 1 mM citalopram indicated that a polypeptide of Mr 73,000 corresponded to the 5-hydroxytryptamine-transporter protein.

IT 144119-27-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(coupling of, to agarose support for purification of sodium-ion-coupled 5-hydroxytryptamine transporter of cerebral cortex)

RN 144119-27-7 CAPLUS
CN 1-Isobenzofuranpropanamine, 5-(aminomethyl)-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (2Z)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

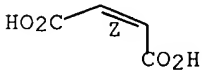
CRN 125803-03-4
CMF C20 H25 F N2 O



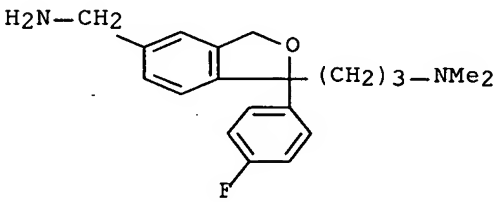
CM 2

CRN 110-16-7
CMF C4 H4 O4

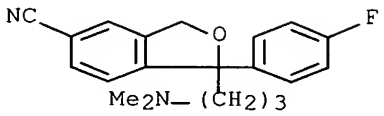
Double bond geometry as shown.



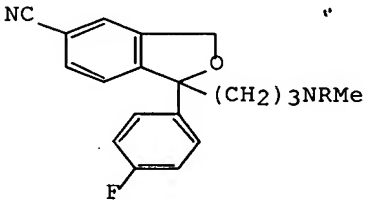
L34 ANSWER 25 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:38592 CAPLUS Full-text
DOCUMENT NUMBER: 114:38592
TITLE: Partial purification of the 5-hydroxytryptamine-reuptake system from human blood platelets using a citalopram-derived affinity resin [Erratum to document cited in CA112(19):175008s]
AUTHOR(S): Biessen, E. A. L.; Robillard, George T.; Horn, A. S.
CORPORATE SOURCE: Subfac. Pharm., Univ. Groningen, Groningen, 9747 AG, Neth.
SOURCE: Biochemistry (1990), 29(41), 9760
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An error in the title of the original article has been corrected The error was reflected in the abstract
IT 125803-03-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with Affi-Gel 10 (Erratum))
RN 125803-03-4 CAPLUS
CN 1-Isobenzofuranpropanamine, 5-(aminomethyl)-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)



IT 59729-33-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reduction of (Erratum))
RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



L34 ANSWER 26 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:631122 CAPLUS Full-text
DOCUMENT NUMBER: 113:231122
TITLE: Synthesis of carbon-11 labeled citalopram, a selective serotonin uptake inhibitor
AUTHOR(S): Ram, Siya
CORPORATE SOURCE: Med. Cent., Duke Univ., Durham, NC, 27710, USA
SOURCE: Applied Radiation and Isotopes (1990), 41(7), 645-8
CODEN: ARISEF; ISSN: 0883-2889
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

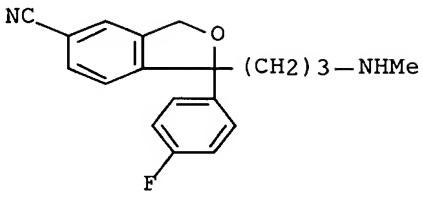


I, R=Me
II, R=H
III, R=$^{11}CH_3$

AB A procedure for labeling the novel serotonin uptake inhibitor, citalopram (I), with the positron emitting radionuclide 11C (t1/2 = 20.4 min) was developed, to permit the pharmacokinetics of this compound to be studied in man. The procedure involves the reaction of 11CH3I with desmethylcitalopram (II) in acetone in the presence of NaOH base at 65° for 8-10 min; this was followed by purification by a column which contained, in series silica gel and basic alumina, and produces no carrier added [11C]citalopram (III) in radiochem. yield (18-66% at EOB) and radiochem. purity (>95%). The specific activity of III was 2.52 + 103-16.06 + 103 GBq/mmol (68-434 Ci/mmol) at the end of synthesis.

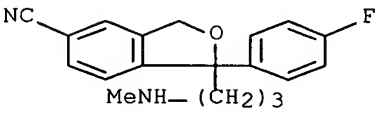
IT 97743-99-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(methylation of, with carbon-11 labeled iodomethane)

RN 97743-99-2 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-(methylamino)propyl]-, hydrochloride (1:1) (CA INDEX NAME)

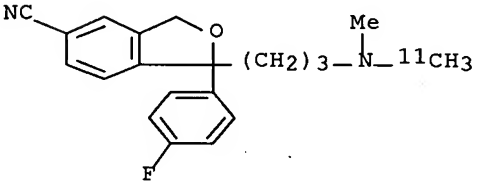


● HCl

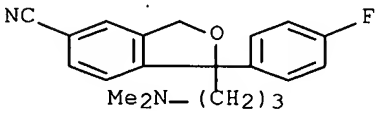
IT 62498-67-3, Desmethylcitalopram
RL: RCT (Reactant); RACT (Reactant or reagent)
(methylation of, with carbon-11 labeled methyliodide)
RN 62498-67-3 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-(methylamino)propyl]- (CA INDEX NAME)



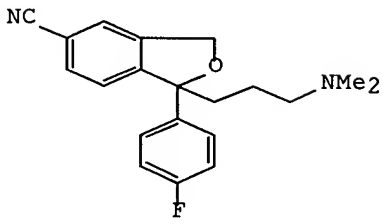
IT 129356-76-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 129356-76-9 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-(methylmethyl-11C-amino)propyl]- (9CI) (CA INDEX NAME)



IT 59729-33-8P, Citalopram
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of carbon-11 labeled and unlabeled)
RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



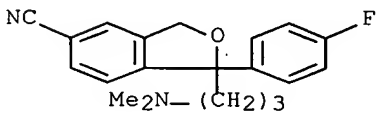
L34 ANSWER 27 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:526655 CAPLUS Full-text
DOCUMENT NUMBER: 113:126655
TITLE: Synthesis of a selective serotonin uptake inhibitor: carbon-11 labeled [11C]citalopram
AUTHOR(S): Dannals, Robert F.; Ravert, Hayden T.; Wilson, Alan A.; Wagner, Henry N., Jr.
CORPORATE SOURCE: Div. Nucl. Med. Radiat. Health Sci., Johns Hopkins Med. Inst., Baltimore, MD, 21205-2179, USA
SOURCE: Applied Radiation and Isotopes (1990), 41(6), 541-3
CODEN: ARISEF; ISSN: 0883-2889
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



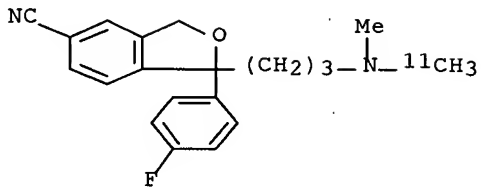
I

AB Citalopram (I), a selective serotonin uptake inhibitor, was labeled with 11C for noninvasive in the human brain using positron emission tomog. The synthesis was completed in .apprx.17 min using [11C]methyl iodide as the precursor. The synthesis, purification, characterization, and determination of specific activity are described.

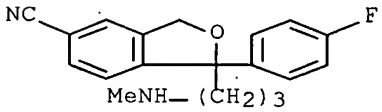
IT 59729-33-8P, Citalopram
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as serotonin uptake inhibitor)
RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



IT 129356-76-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as serotonin uptake inhibitor, for PET)
RN 129356-76-9 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-(methylmethyl-11C-amino)propyl]- (9CI) (CA INDEX NAME)



IT 62498-67-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with Me iodide)
RN 62498-67-3 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-(methylamino)propyl]- (CA INDEX NAME)



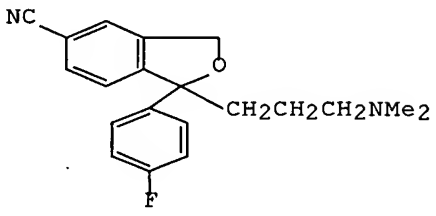
L34 ANSWER 28 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:478150 CAPLUS Full-text
DOCUMENT NUMBER: 113:78150
TITLE: Preparation and isolation of antidepressant drug citalopram enantiomers and their pharmaceutical compositions
INVENTOR(S): Boegesoe, Klaus Peter; Perregaard, Jens
PATENT ASSIGNEE(S): Lundbeck, H., og Co. A/S, Den.
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 347066	A1	19891220	EP 1989-305532	19890601 <--
EP 347066	B1	19950315		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8902599	A	19891215	DK 1989-2599	19890529 <--
IL 90465	A	19950124	IL 1989-90465	19890530 <--
AT 119896	T	19950415	AT 1989-305532	19890601 <--
ES 2068891	T3	19950501	ES 1989-305532	19890601 <--
FI 8902823	A	19891215	FI 1989-2823	19890608 <--
FI 91527	B	19940331		
FI 91527	C	19940711		
US 4943590	A	19900724	US 1989-363589	19890608 <--
NO 8902447	A	19891215	NO 1989-2447	19890613 <--
NO 172892	B	19930614		
NO 172892	C	19930922		
AU 8936295	A	19900104	AU 1989-36295	19890613 <--
AU 623144	B2	19920507		

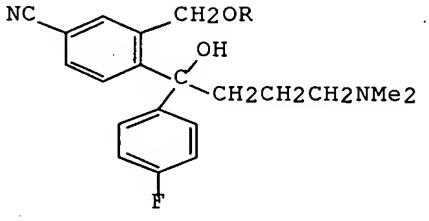
ZA 8904476	A	19900425	ZA 1989-4476		19890613 <--
CA 1339452	C	19970909	CA 1989-602683		19890613 <--
JP 02036177	A	19900206	JP 1989-149752		19890614 <--
JP 3044253	B2	20000522			
DK 9300115	A	19930201	DK 1993-115		19930201 <--
DK 170280	B1	19950724			
US 34712	E	19940830	US 1993-122009		19930914 <--
FI 9401829	A	19940420	FI 1994-1829		19940420 <--
FI 113762	B1	20040615			
CA 1339568	C	19971202	CA 1997-617069		19970122 <--
JP 11292867	A	19991026	JP 1999-46008		19990224 <--
JP 3038204	B2	20000508			
FI 2000000507	A	20000306	FI 2000-507		20000306 <--
FI 2004001359	A	20041020	FI 2004-1359		20041020
PRIORITY APPLN. INFO.:			GB 1988-14057	A	19880614
			FI 1989-2823	A	19890608
			US 1989-363589	A5	19890608
			CA 1989-602683	A3	19890613
			JP 1989-149752	A3	19890614

OTHER SOURCE(S): MARPAT 113:78150

GI



I



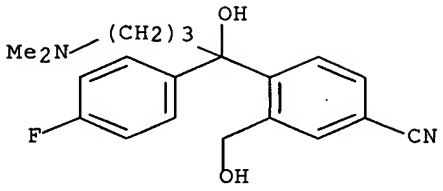
II

AB The title compound (I) in pure (+)-enantiomer form and its racemic mixture, useful as antidepressants, geriatrics, or in treatment of obesity and alcoholism, are prepared SOCl2 was refluxed with a solution of (+)-CF3CH(OMe)CO2H in CHCl3 to give the acid chloride, which was diluted with CH2Cl2 and treated with benzyl alc. derivative II (R = H) and Et3N to give ester II [R = CF3CH(OMe)CO] (III) as a diastereomeric mixture, which was purified by HPLC to give a pure enantiomer. III was dissolved in MePh and treated with Me3COK in MePh at 0° to give (+)-I of 99.6% optical purity, which showed ED50 of 2.0 μmol/kg for 5-HTP potentiation in mice and IC50 of 1.1 nM against 5-HT uptake, vs. 3.3 μmol/kg and 1.8 μM, resp., with (±)-I. Similarly prepd . (-)-I showed much lower activity. Tablet, syrup, and injection formulations were given.

IT 103146-25-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of)

RN 103146-25-4 CAPLUS

CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)

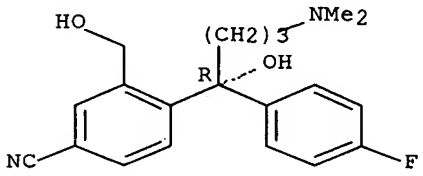


IT 219861-19-5P 219861-52-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and conversion to free base)
RN 219861-19-5 CAPLUS
CN Benzonitrile, 4-[(1R)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)-, (2R,3R)-2,3-dihydroxybutanedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 481047-48-7
CMF C20 H23 F N2 O2

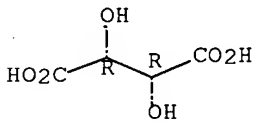
Absolute stereochemistry. Rotation (+).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

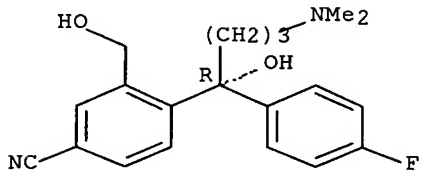


RN 219861-52-6 CAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with 4-[(1R)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 481047-48-7
CMF C20 H23 F N2 O2

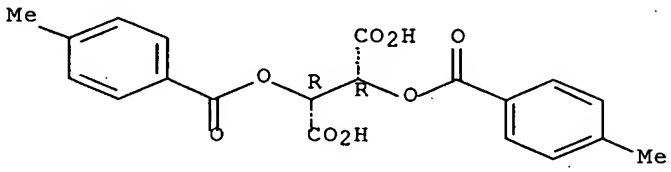
Absolute stereochemistry. Rotation (+).



CM 2

CRN 32634-66-5
CMF C20 H18 O8

Absolute stereochemistry. Rotation (-).

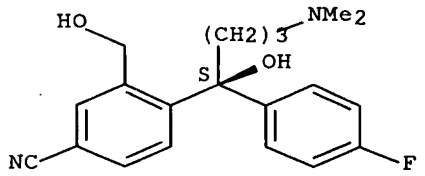


IT 128173-53-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of)
RN 128173-53-5 CAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2S,3S)-, compd. with 4-[(1S)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)benzonitrile (1:2) (CA INDEX NAME)

CM 1

CRN 488787-59-3
CMF C20 H23 F N2 O2

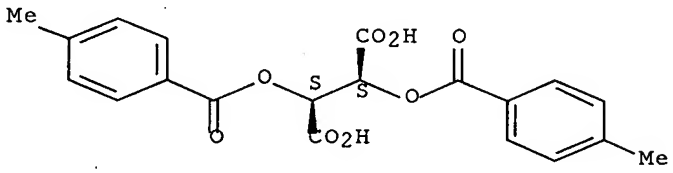
Absolute stereochemistry. Rotation (-).



CM 2

CRN 32634-68-7
CMF C20 H18 O8

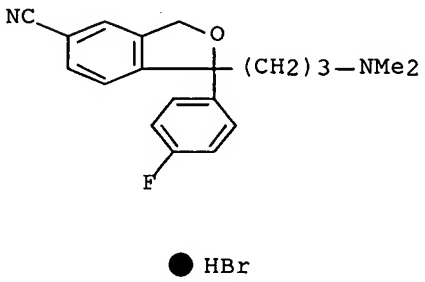
Absolute stereochemistry. Rotation (+).



IT 59729-32-7P 59729-33-8P 128196-01-0P
128196-02-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antidepressant)

RN 59729-32-7 CAPLUS

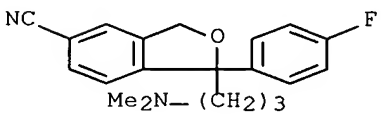
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)



● HBr

RN 59729-33-8 CAPLUS

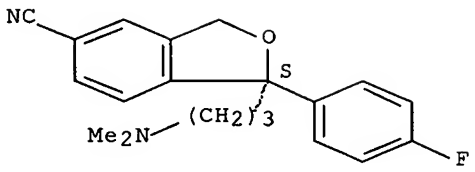
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



RN 128196-01-0 CAPLUS

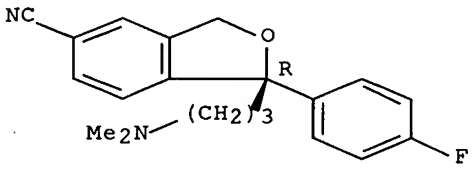
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 128196-02-1 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

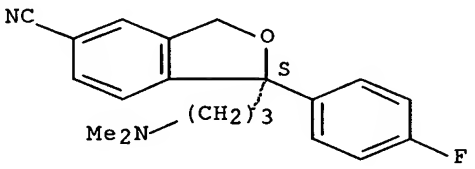


IT 219861-08-2P 219861-09-3P 219861-53-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antidepressant)
RN 219861-08-2 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1), (1S)- (CA INDEX NAME)

CM 1

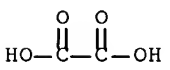
CRN 128196-01-0
CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (+).



CM 2

CRN 144-62-7
CMF C2 H2 O4

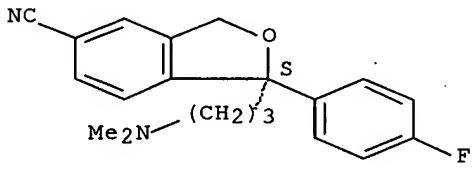


RN 219861-09-3 CAPLUS
CN 2-Naphthalenecarboxylic acid, 4,4'-methylenebis[3-hydroxy-, compd. with (1S)-1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile (1:2) (9CI) (CA INDEX NAME)

CM 1

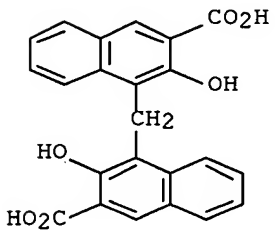
CRN 128196-01-0
CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (+).



CM 2

CRN 130-85-8
CMF C23 H16 O6

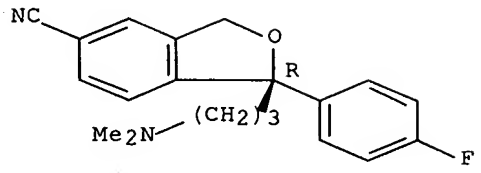


RN 219861-53-7 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1R)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

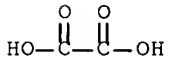
CRN 128196-02-1
CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (-).

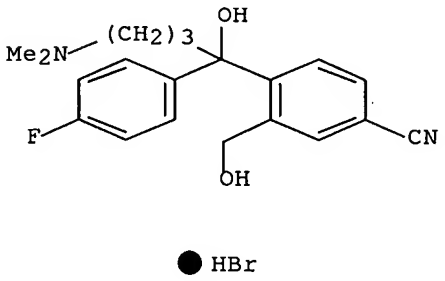


CM 2

CRN 144-62-7
CMF C2 H2 O4



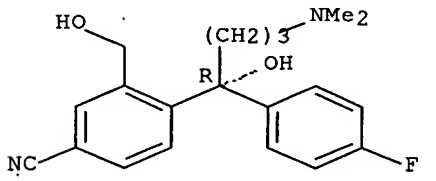
IT 103146-26-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(resolution via conversion to di-(p-toloyl)tartrate salt)
RN 103146-26-5 CAPLUS
CN Benzonitrile, 4-[4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)-, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

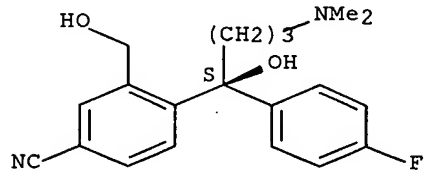
IT 481047-48-7P 488787-59-3P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(separation from enantiomer and cyclization of)
RN 481047-48-7 CAPLUS
CN Benzonitrile, 4-[(1R)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

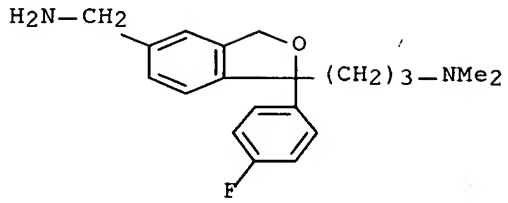


RN 488787-59-3 CAPLUS
CN Benzonitrile, 4-[(1S)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)

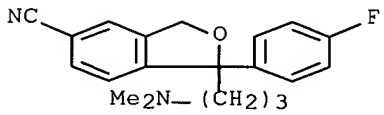
Absolute stereochemistry. Rotation (-).



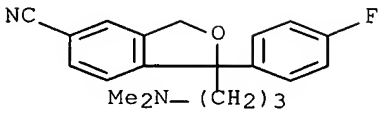
L34 ANSWER 29 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:175008 CAPLUS Full-text
DOCUMENT NUMBER: 112:175008
TITLE: Partial purification of the 5-hydroxytryptophan-reuptake system from human blood platelets using a citalopram-derived affinity resin
AUTHOR(S): Biessen, E. A. L.; Robillard, George T.; Horn, A. S.
CORPORATE SOURCE: Subfac. Pharm., Univ. Groningen, Groningen, 9747 AG, Neth.
SOURCE: Biochemistry (1990), 29(13), 3349-54
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A 2-step scheme was developed for partial purification, based on wheat-germ agglutinin-lectin (WGA) affinity chromatog. and citalopram affinity chromatog. Upon solubilization of the carrier with 1% digitonin, a 50-70-fold increase in specific [3H]imipramine-binding activity with 70% recovery was accomplished with WGA-lectin chromatog. The WGA pool then was subjected to affinity chromatog. on newly synthesized citalopram-agarose. At least 90% of the binding capacity adsorbed to the column. Specific elution with 10 μM citalopram resulted in a 22% recovery of binding activity. A 10,000-fold overall purification was obtained by using this 2-step procedure. Anal. of the fractions on SDS-PAGE after 125I labeling revealed specific elution of 78- and 55-kilodaltons proteins concomitant with the appearance of [3H]imipramine-binding activity. The pharmacol. profile of the partially purified reuptake system correlated well with that derived from the crude membrane-bound reuptake system, suggesting a copurifn. of the 5-HT-binding activity and [3H]imipramine-binding activity.
IT 125803-03-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with Affi-Gel 10)
RN 125803-03-4 CAPLUS
CN 1-Isobenzofuranpropanamine, 5-(aminomethyl)-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)



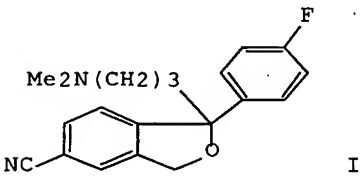
IT 59729-33-8, Citalopram
RL: RCT (Reactant); RACT (Reactant or reagent)
(reduction of)
RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



L34 ANSWER 30 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:181994 CAPLUS Full-text
DOCUMENT NUMBER: 104:181994
TITLE: Solubilization and characterization of the 5-hydroxytryptamine transporter complex from rat cerebral cortical membranes
AUTHOR(S): Habert, Estelle; Graham, David; Langer, Salomon Z.
CORPORATE SOURCE: Lab. Etud. Rech. Synth., Paris, 75013, Fr.
SOURCE: European Journal of Pharmacology (1986), 122(2), 197-204
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 5-hydroxytryptamine transporter complex from rat cerebral cortical membranes was solubilized with digitonin. The affinity of the solubilized transporter complex for [3H]paroxetine, a very selective and potent inhibitor of 5-hydroxytryptamine uptake, was not affected and remained unchanged when compared with the parent membrane preparation The solubilization yield of membrane-bound [3H]paroxetine-binding sites was 42%. The pharmacol. profile of the solubilized transporter complex was similar to that of the intact transporter in membranes of the cerebral cortex, with the exception of tryptamine, which was 10-fold less potent in inhibition of [3H]paroxetine binding to the solubilized transporter when compared to membranes. The Stokes' radius of the complex, determined by gel filtration, was 7.6 nm. This successful solubilization of the neuronal 5-hydroxytryptamine transporter complex is the starting point for purification of this macromol. moiety.
IT 59729-33-8
RL: BIOL (Biological study)
(hydroxytryptamine transporter complex of cerebral cortex membranes binding of hydroxytryptamine inhibition by, kinetics of)
RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



L34 ANSWER 31 OF 31 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1982:96989 CAPLUS Full-text
DOCUMENT NUMBER: 96:96989
TITLE: Determination of the antidepressant agent citalopram and metabolites in plasma by liquid chromatography with fluorescence detection
AUTHOR(S): Oeyehaug, Ellen; Oestensen, Eilif Terje; Salvesen, Bjarne
CORPORATE SOURCE: Agder Coll., Kristiansand, 4600, Norway
SOURCE: Journal of Chromatography (1982), 227(1), 129-35
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



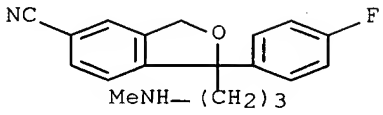
I

AB A high-performance liquid chromatog. method is described for the determination of citalopram (I) [59729-33-8] (the methylamino [62498-67-3] and amino [62498-69-5] derivs.) and its two main metabolites. The compds. were extracted from alkaline plasma with di-Et ether. The combined ether layers were evaporated after addition of 50 μL of 0.1 N HCl. The residual exts. were purified with di-Et ether and 20 μL were injected into a Spherisorb ODS 5-μm column with MeCN-0.6% phosphate buffer pH 3 (55:45, volume/volume) as the mobile phase. Using a fluorescence detector, the detection limits are 1 ng/mL of plasma for citalopram and the methylamino metabolite and 0.5 ng/mL for the amino metabolite.

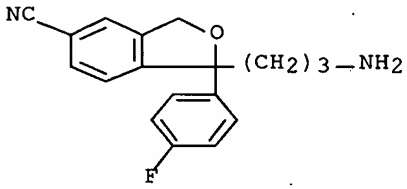
IT 62498-67-3 62498-69-5
RL: PROC (Process)
(as citalopram metabolite, determination of, in blood plasma of human by high-performance liquid chromatog.)

RN 62498-67-3 CAPLUS

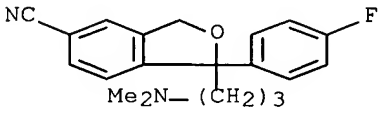
CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-(methylamino)propyl]- (CA INDEX NAME)



RN 62498-69-5 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-(3-aminopropyl)-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



IT 59729-33-8
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood plasma of human by high-performance liquid chromatog., metabolites in relation to)
RN 59729-33-8 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (CA INDEX NAME)



L35 194 MEI R?/AU

L36 2248 GUO D?/AU

L37 35931 WANG S?/AU

=> s l35 and l36 and l37
L38 1 L35 AND L36 AND L37

=> d ibib abs hitstr

L38 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1075785 CAPLUS Full-text
DOCUMENT NUMBER: 143:347046
TITLE: Preparation of crystalline citalopram diol intermediate
INVENTOR(S): Mei, Runan; Guo, Dianwu;

Wang, Shulong
PATENT ASSIGNEE(S): Hangzhou Minsheng Pharmaceutical Co., Ltd, Peop. Rep. China
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005092875	A1	20051006	WO 2004-CN1418	20041206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1629153	A	20050622	CN 2004-10044335	20040526
EP 1700851	A1	20060913	EP 2004-802432	20041206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
US 2007117992	A1	20070524	US 2006-583360	20060619

PRIORITY APPLN. INFO.: CN 2003-10123623 A 20031219
CN 2004-10044335 A 20040526
WO 2004-CN1418 W 20041206

OTHER SOURCE(S): MARPAT 143:347046
AB The invention relates to the diol intermediate of citalopram useful for treatment of depression, that is to say, the crystal of free base of 3-hydroxymethyl-4-[1-(4-fluorophenyl)-1-hydrorybutyl-4-(dimethylamino)]butylbenzonitrile, and the method of crystallization thereof. The invention has disclosed the method to prepare the pure citalopram, its purified salts, the optical resolution method of citalopram diol intermediate, the method to prepare S-citalopram and its purified salts by crystals mentioned above. The invention has also disclosed citalopram and its purified salts, (S)-citalopram and its purified salts, as well as pharmaceutical formulation thereof obtained. Using methods of the invention, the quality and yield of the product can be signally improved, and production cost of the medicinal material can be decreased.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> dis his nofile

(FILE 'HOME' ENTERED AT 18:10:43 ON 19 SEP 2007)

FILE 'REGISTRY' ENTERED AT 18:10:48 ON 19 SEP 2007

L1 STR
L2 STR L1
L3 16 SEA SSS SAM L1 OR L2
L4 STR L1
L5 STR L***
L6 28 SEA SSS SAM L4 OR L5

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L7          454 SEA SSS FUL L4 OR L5
                D L7 QUE STAT

     FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 18:15:00 ON 19 SEP 2007
L8         1914 SEA ABB=ON  PLU=ON  L7
L9         2783 SEA ABB=ON  PLU=ON  L7
L10        9065 SEA ABB=ON  PLU=ON  L7
L11        2372 SEA ABB=ON  PLU=ON  L7
     TOTAL FOR ALL FILES
L12       16134 SEA ABB=ON  PLU=ON  L7
L13         679 SEA ABB=ON  PLU=ON  L8 AND (METHOD OR PREP?)
L14        1181 SEA ABB=ON  PLU=ON  L9 AND (METHOD OR PREP?)
L15        1786 SEA ABB=ON  PLU=ON  L10 AND (METHOD OR PREP?)
L16         923 SEA ABB=ON  PLU=ON  L11 AND (METHOD OR PREP?)
     TOTAL FOR ALL FILES
L17        4569 SEA ABB=ON  PLU=ON  L12 AND (METHOD OR PREP?)
L18      868119 SEA ABB=ON  PLU=ON  CRYSTALL? OR PURIF?
L19      462956 SEA ABB=ON  PLU=ON  CRYSTALL? OR PURIF?
L20      316868 SEA ABB=ON  PLU=ON  CRYSTALL? OR PURIF?
L21     1768748 SEA ABB=ON  PLU=ON  CRYSTALL? OR PURIF?
     TOTAL FOR ALL FILES
L22     3416691 SEA ABB=ON  PLU=ON  CRYSTALL? OR PURIF?
L23           8 SEA ABB=ON  PLU=ON  L13 AND L18
L24          20 SEA ABB=ON  PLU=ON  L14 AND L19
L25          12 SEA ABB=ON  PLU=ON  L15 AND L20
L26          62 SEA ABB=ON  PLU=ON  L16 AND L21
     TOTAL FOR ALL FILES
L27         102 SEA ABB=ON  PLU=ON  L17 AND L22

     FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 18:16:39 ON 19 SEP 2007
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L29          20 SEA ABB=ON  PLU=ON  L14 AND L19
L30          12 SEA ABB=ON  PLU=ON  L15 AND L20
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L32          33 DUP REM L31 (7 DUPLICATES REMOVED)
                D 1-33 IBIB ABS

     FILE 'CAPLUS' ENTERED AT 18:17:07 ON 19 SEP 2007
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L36        2248 SEA ABB=ON  PLU=ON  GUO D?/AU
L37       35931 SEA ABB=ON  PLU=ON  WANG S?/AU
L38           1 SEA ABB=ON  PLU=ON  L35 AND L36 AND L37
                D IBIB ABS HITSTR

=> s (135 or 136 or 137) and 17
          2372 L7
L39          3 (L35 OR L36 OR L37) AND L7

=> s 139 not 138
L40          2 L39 NOT L38

=> d 1-2 ibib abs hitstr

L40  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:613975  CAPLUS  Full-text
DOCUMENT NUMBER:          147:118028
```

TITLE: Process for preparation of chiral diols and esters as citalopram intermediates

INVENTOR(S): Wang, Shizhen; Yang, Lirong; Wu, Jianping; Xu, Gang

PATENT ASSIGNEE(S): Zhejiang University, Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 11pp.
CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

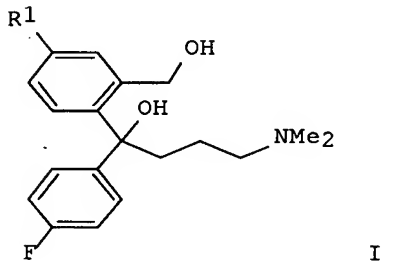
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

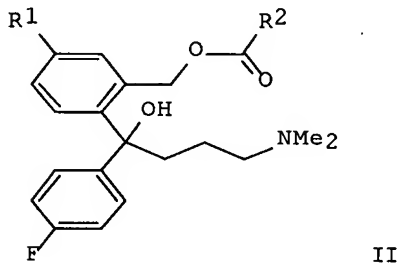
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1974542	A	20070606	CN 2006-10155058	20061207

PRIORITY APPLN. INFO.: CN 2006-10155058 20061207

GI



I



II

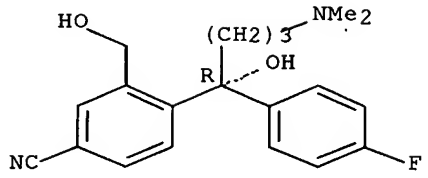
AB This invention pertains to a method for producing chiral diols I and esters II [wherein R1 = CN or a group that can be transformed to CN; R2 = (un)substituted alkyl, alkenyl, or alkynyl] as citalopram intermediates. The title method comprises: (1) adding 0.001-0.05 mol ester, 0.002-0.2 mol alc., and 10-500 mL organic solvent containing 0-1% water into a reactor, and (2) adding 25-1,500 mg lipase, and carrying out reaction at 0-70 °C for 30-180 h to obtain the final products. This method has the advantages of good reaction selectivity, high conversion rate, wide range of reaction temperature, simple process, simple equipment, stable enzyme activity, and recyclable enzyme. The obtained S- or R-diol and esters have high optical purity.

IT 481047-48-7P 488787-59-3P
RL: BPN (Biosynthetic preparation); IMF (Industrial manufacture); BIOL (Biological study); PREP (Preparation)
(preparation of chiral diols and esters as citalopram intermediates)

RN 481047-48-7 CAPLUS

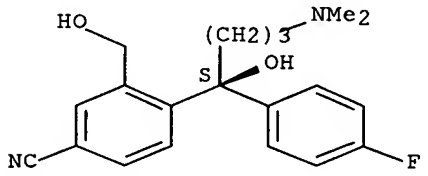
CN Benzonitrile, 4-[(1R)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 488787-59-3 CAPLUS
CN Benzonitrile, 4-[(1S)-4-(dimethylamino)-1-(4-fluorophenyl)-1-hydroxybutyl]-3-(hydroxymethyl)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



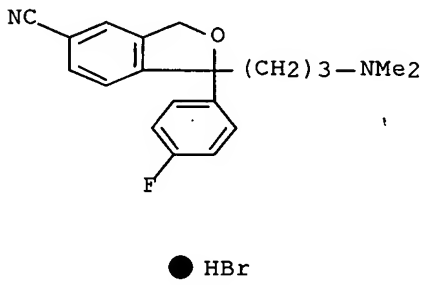
L40 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:186451 CAPLUS Full-text
DOCUMENT NUMBER: 146:302242
TITLE: Method for manufacturing citalopram hydrobromide oral liquid with improved stability
INVENTOR(S): Wang, Sunan; Zhang, Sumin; Dong, Jiali; Wang, Xianliang; Xu, Junjun
PATENT ASSIGNEE(S): Shanghai Industrial United Holdings Great Wall Pharmaceutical Co., Ltd., Peop. Rep. China; Shanghai Industrial United Holdings Pharmaceutical Research Co., Ltd.
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 10pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1911207	A	20070214	CN 2006-10030979	20060908
PRIORITY APPLN. INFO.:			CN 2006-10030979	20060908

AB The title oral liquid is composed of (by weight%) citalopram hydrobromide 0.01-1, sweetening agent and plasticizing agent 12-35, preservative 0.01-0.5, aromatic 0.005-0.05, and solvent 64-87. The sweetening agent and plasticizing agent are selected from sorbitol, glycerol, and propylene glycol. The preservative is selected from methyl-p-hydroxybenzoate, propyl-p-hydroxybenzoate, benzoic acid, and sodium benzoate. The aromatic can be mint essence, orange essence, and strawberry essence. The oral liquid has increased sweetness, less bitterness, and good stability.

IT 59729-32-7, Citalopram hydrobromide
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for manufacturing citalopram hydrobromide oral liquid with improved

stability)
RN 59729-32-7 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, hydrobromide (1:1) (CA INDEX NAME)

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=> e citalopram/cn 5
E1            1     CITALBA R/CN
E2            1     CITALDOXIME/CN
E3            1 --> CITALOPRAM/CN
E4            1     CITALOPRAM ACETATE/CN
E5            1     CITALOPRAM HYDROBROMIDE/CN

=> s ?citalopram?/cns
L41          21 ?CITALOPRAM?/CNS

=> fil medl,biosis,embase,caplus;s (l41 or citalopram?)(l)crystal?
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L42             4 FILE MEDLINE
L43             7 FILE BIOSIS
L44             4 FILE EMBASE
L45            38 FILE CAPLUS

TOTAL FOR ALL FILES
L46            53 (L41 OR CITALOPRAM?)(L) CRYSTAL?

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L48             7 FILE BIOSIS
L49             4 FILE EMBASE
L27 NOT FOUND

=> fil medl,biosis,embase

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L51             7 FILE BIOSIS
L52             4 FILE EMBASE

TOTAL FOR ALL FILES
L53            15 L46 NOT (L38 OR L39 OR L31)

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PROCESSING COMPLETED FOR L53
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In a multifile environment, a format can only be used if it is valid
in at least one of the files.  Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end

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L54 ANSWER 1 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:346542 BIOSIS Full-text
DOCUMENT NUMBER: PREV200600345674
TITLE: Identification of residues in the serotonin transporter engaged in high affinity recognition of antidepressants and cocaine.
AUTHOR(S): Field, Julie R. [Reprint Author]; Henry, L. Keith; Dawson, Eric S.; Blakely, Randy D.
CORPORATE SOURCE: Vanderbilt Univ, Ctr Mol Neuro, Med Ctr, Nashville, TN 37232 USA
SOURCE: FASEB Journal, (MAR 6 2006) Vol. 20, No. 4, Part 1, pp. A683.
Meeting Info.: Experimental Biology 2006 Meeting. San Francisco, CA, USA. April 01 -05, 2006. Amer Assoc Anatomists; Amer Physiol Soc; Amer Soc Biochem & Mol Biol; Amer Soc Investigat Pathol; Amer Soc Nutr; Amer Soc Pharmacol & Expt Therapeut.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Jul 2006
Last Updated on STN: 12 Jul 2006

AB The serotonin (5HT) transporter (SERT) is an important target for antidepressants and psychostimulants, including cocaine and ecstasy. Using an evolutionary comparison of human and Drosophila SERTs, we have identified residues in transmembrane segments (TM) 1 and 3 that influence 5HT and competitor interactions. In TM 3, replacement of isoleucine at hSERT position 172 with methionine, the residue native to dSERT, discriminates between 5HT and antagonists, demonstrating no effect on substrate potency while causing a thousand-fold loss of potency for citalopram, as well as significant losses in potency for several selective serotonin reuptake inhibitors, tricyclic antidepressants, and cocaine. Importantly, the reciprocal mutation in dSERT, M1671, shows a significant gain of potency for citalopram, fluoxetine and cocaine, but no change in 5HT uptake properties. hSERT 1172 may coordinate citalopram binding with a previously identified TM I residue Y95, as hSERT Y95F/1172M shows a synergistic loss in citalopram potency. The proximity of these residues is supported by the recent crystal structure of an hSERT bacterial ortholog, the leucine transporter LeuT(Aa). Our data support a potential for these residues to coordinate antidepressant and substrate binding and offer new insights into mechanisms of ligand selectivity among biogenic amine neurotransmitter transporters.

L54 ANSWER 2 OF 7 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2005656010 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16216517
TITLE: Putative drug binding conformations of monoamine transporters.
AUTHOR: Ravna Aina Westrheim; Sylte Ingebrigt; Kristiansen Kurt; Dahl Svein G
CORPORATE SOURCE: Department of Pharmacology, Institute of Medical Biology, University of Tromso, N-9037 Tromso, Norway.. aina@fagmed.uit.no
SOURCE: Bioorganic & medicinal chemistry, (2006 Feb 1) Vol. 14, No. 3, pp. 666-75. Electronic Publication: 2005-10-10.
Journal code: 9413298. ISSN: 0968-0896.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200604
ENTRY DATE: Entered STN: 18 Dec 2005
Last Updated on STN: 21 Apr 2006
Entered Medline: 20 Apr 2006

AB Structural information about monoamine transporters and their interactions with psychotropic drugs is important for understanding their molecular mechanisms of action and for drug development. The crystal structure of a Major Facilitator Superfamily (MFS) transporter, the lactose permease symporter (lac permease), has provided insight into the three-dimensional structure and mechanisms of secondary transporters. Based on the hypothesis that the 12 transmembrane alpha-helix (TMH) secondary transporters belong to a common folding class, the lac permease structure was used for molecular modeling of the serotonin transporter (SERT), the dopamine transporter (DAT), and the noradrenaline transporter (NET). The molecular modeling methods used included amino acid sequence alignment, homology modeling, and molecular mechanical energy calculations. The lac permease crystal structure has an inward-facing conformation, and construction of outward-facing SERT, DAT, and NET conformations allowing ligand binding was the most challenging step of the modeling procedure. The psychomotor stimulants cocaine and S-amphetamine, and the selective serotonin reuptake inhibitor (SSRI) S- citalopram, were docked into putative binding sites on the transporters to examine their molecular binding mechanisms. In the inward-facing conformation of SERT the translocation pore was closed towards the extracellular side by hydrophobic interactions between the conserved amino acids Phe105, Pro106, Phe117, and Ala372. An unconserved amino acid, Asp499 in TMH10 in NET, may contribute to the low affinity of S-citalopram to NET.

L54 ANSWER 3 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:548051 BIOSIS Full-text
DOCUMENT NUMBER: PREV200510345741
TITLE: Pharmaceutical composition containing citalopram.
AUTHOR(S): Liljegren, Ken [Inventor]; Holm, Per [Inventor]; Nielsen, Ole [Inventor]; Wagner, Sven [Inventor]
CORPORATE SOURCE: Vaerlose, Denmark
ASSIGNEE: H. Lundbeck A/S
PATENT INFORMATION: US 06849659 20050201
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (FEB 1 2005)
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Dec 2005
Last Updated on STN: 7 Dec 2005

AB A solid unit dosage form comprising citalopram, which is prepared by direct compression of a mixture of citalopram base or a pharmaceutically acceptable salt thereof and pharmaceutically acceptable excipients, or by filling of said mixture in a hard gelatine capsule. Large crystals of a pharmaceutical acceptable salt of citalopram and method for the manufacture of said large crystals.

L54 ANSWER 4 OF 7 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003250613 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12747792
TITLE: Interaction of cis-(6-benzhydrylpiperidin-3-yl)benzylamine analogues with monoamine transporters: structure-activity relationship study of structurally constrained

3,6-disubstituted piperidine analogues of (2,2-diphenylethyl)-[1-(4-fluorobenzyl)piperidin-4-ylmethyl]amine.

AUTHOR: Kolhatkar Rohit B; Ghorai Sujit K; George Clifford; Reith Maarten E A; Dutta Aloke K

CORPORATE SOURCE: Wayne State University, Department of Pharmaceutical Sciences, Detroit, Michigan 48202, USA.

CONTRACT NUMBER: DA 12449 (NIDA)

SOURCE: Journal of medicinal chemistry, (2003 May 22) Vol. 46, No. 11, pp. 2205-15.
Journal code: 9716531. ISSN: 0022-2623.

PUB. COUNTRY: United States

DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200306

ENTRY DATE: Entered STN: 31 May 2003
Last Updated on STN: 24 Jun 2003
Entered Medline: 23 Jun 2003

AB To explore structure-activity relationships (SAR) of a novel conformationally constrained lead cis-3,6-disubstituted piperidine derivative derived from (2,2-diphenylethyl)-[1-(4-fluorobenzyl)piperidine- 4-ylmethyl]amine (I), a series of compounds was synthesized by derivatizing the exocyclic N-atom at the 3-position of the lead. This study led to the formation of substituted phenyl and heterocyclic derivatives. All novel compounds were tested for their affinity at the dopamine transporter (DAT), serotonin transporter (SERT), and norepinephrine transporter (NET) in the brain by measuring their potency in competing for the binding of [3H]WIN 35 428, [3H]citalopram, and [3H]nisoxetine, respectively. Selected compounds were also evaluated for their activity in inhibiting the uptake of [3H]DA. The SAR results demonstrated that the nature of substitutions on the phenyl ring is important in activity at the DAT with the presence of an electron-withdrawing group having the maximum effect on potency. Replacement of the phenyl ring in the benzyl group by heterocyclic moieties resulted in the development of compounds with moderate activity for the DAT. Two most potent racemic compounds were separated by a diastereoisomeric separation procedure, and differential affinities were observed for the enantiomers. Absolute configuration of the enantiomers was obtained unambiguously by X-ray crystal structural study. One of the enantiomers, compound S,S-(-)-19a, exhibited the highest potency for the DAT (IC50 = 11.3 nM) among all the compounds tested and was as potent as GBR 12909 (1-[2-[bis(4-fluorophenyl)methoxy]ethyl]-4-(3-phenylpropyl)piperazine). However, the compound (-)-19a was more selective than GBR 12909 in binding to the DAT compared with binding to the SERT and NET. The present results establish the newly developed 3,6-disubstituted piperidine derivatives as a novel template for high-affinity inhibitors of DAT. Structurally these molecules are more constrained compared to our earlier flexible piperidine molecules and, thus, should provide more insights about their bioactive conformations.

L54 ANSWER 5 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:596570 BIOSIS Full-text

DOCUMENT NUMBER: PREV200200596570

TITLE: Method for the preparation of pure citalopram.

AUTHOR(S): Villa, Marco [Inventor, Reprint author]; Sbrogio , Federico [Inventor]; Dancer, Robert [Inventor]

CORPORATE SOURCE: Padova, Italy
ASSIGNEE: H. Lundbeck A/S, Valby-Copenhagen, Denmark

PATENT INFORMATION: US 6455710 20020924
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 24, 2002) Vol. 1262, No. 4. http://www.uspto.gov/web/menu/patdata.html. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Nov 2002
Last Updated on STN: 20 Nov 2002

AB The present invention relates to the process for the preparation and purification of citalopram (I) ##STR1## in which a compound of formula (II) ##STR2## wherein Z is iodo, bromo, chloro or CF3 --(CF2)n --SO2 --O--, n being 0, 1, 2, 3, 4, 5, 6, 7 or 8, is subjected to a cyanide exchange reaction with a cyanide source; the resultant crude citalopram product is optionally subjected to some initial purification and subsequently treated with an amide or an amide-like group forming agent; the reaction mixture is then subjected to an acid/base wash and/or crystallisation and recrystallisation of citalopram in order to remove the amides formed from the crude citalopram mixture; and the resulting citalopram product is optionally further purified, worked up and isolated as the base or a pharmaceutically acceptable salt thereof.

L54 ANSWER 6 OF 7 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2001150990 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11170654
TITLE: Structure-activity relationships at monoamine transporters and muscarinic receptors for N-substituted-3alpha-(3'-chloro-, 4'-chloro-, and 4',4''-dichloro-substituted-diphenyl)methoxytropanes.
AUTHOR: Newman A H; Robarge M J; Howard I M; Wittkopp S L; George C; Kopajtic T; Izenwasser S; Katz J L
CORPORATE SOURCE: Medicinal Chemistry and Psychobiology Sections, National Institute on Drug Abuse-Intramural Research Program, Baltimore, Maryland 21224, USA.. anewman@intra.nida.nih.gov
CONTRACT NUMBER: DA09045 (NIDA)
SOURCE: Journal of medicinal chemistry, (2001 Feb 15) Vol. 44, No. 4, pp. 633-40.
Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 4 Apr 2001
Last Updated on STN: 4 Apr 2001
Entered Medline: 15 Mar 2001

AB The design, synthesis, and evaluation of 3alpha-(diphenylmethoxy)tropane (benztropine) analogues have provided potent and selective probes for the dopamine transporter. Structure-activity relationships (SARs) have been developed that contrast with those described for cocaine, despite significant structural similarity. Furthermore, behavioral evaluation of many of the benztropine analogues in animal models of cocaine abuse has suggested that these two classes of tropane-based dopamine uptake inhibitors have distinct pharmacological profiles. In general, the benztropine analogues do not demonstrate efficacious locomotor stimulation in mice, do not fully substitute for a cocaine discriminative stimulus, and are not appreciably self-

administered in rhesus monkeys. These compounds are generally more potent than cocaine as dopamine uptake inhibitors in vitro, although their actions in vivo are not consistent with this action. These observations suggest that differing binding profiles at the serotonin and norepinephrine transporters as well as at muscarinic receptors might have significant impact on the pharmacological actions of these compounds. In addition, by varying the structures of the parent compounds and thereby modifying their physical properties, pharmacokinetics as well as pharmacodynamics will be directly affected. Therefore, in an attempt to systematically evaluate the impact of chemical modification on these actions, a series of N-substituted (H, CH3, allyl, benzyl, propylphenyl, and butylphenyl) analogues of 3'-chloro-, 4'-chloro-, and 4,4''-dichloro-3alpha-(diphenylmethoxy)tropanes were synthesized. These compounds were evaluated for displacement, in rat tissue, of [3H]WIN 35,428 from the dopamine transporter, [3H] citalopram from the serotonin transporter, [3H]nisoxetine from the norepinephrine transporter, and [3H]pirenzepine from muscarinic m1 receptors. SARs were developed and compared to a series of N-substituted-3alpha-(bis-4'-fluorophenyl)methoxytropanes. The present SARs followed previously reported studies with the single exception of the N-butylphenyl substituent, which did not provide the high affinity binding in any of these three sets of analogues, as it did in the 4',4''-difluoro series. X-ray crystallographic analyses of the three parent ligands (1a, 2a, and 3a) were compared to that of 3alpha-(bis-4'- fluorophenyl)methoxytropane which provided supportive evidence toward the proposal that the combination of steric bulk in both the 3-position and the N-substituent, in this class of compounds, is not optimal for binding at the dopamine transporter. These studies provide binding profile data that can now be used to correlate with future behavioral analyses of these compounds and may provide insight into the kind of binding profile that might be targeted as a potential treatment for cocaine abuse.

L54 ANSWER 7 OF 7 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2000135969 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10669578
TITLE: New selective and potent 5-HT(1B/1D) antagonists: chemistry and pharmacological evaluation of N-piperazinylphenyl biphenylcarboxamides and biphenylsulfonamides.
AUTHOR: Liao Y; Bottcher H; Harting J; Greiner H; van Amsterdam C; Cremers T; Sundell S; Marz J; Rautenberg W; Wikstrom H
CORPORATE SOURCE: Department of Medicinal Chemistry, University of Groningen, A. Deusinglaan 1, NL-9713 AV Groningen, The Netherlands.. y.liao@farm.rug.nl
SOURCE: Journal of medicinal chemistry, (2000 Feb 10) Vol. 43, No. 3, pp. 517-25.
Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 27 Mar 2000
Last Updated on STN: 27 Mar 2000
Entered Medline: 13 Mar 2000

AB A series of new analogues of N-[4-methoxy-3-(4-methylpiperazin-1-yl)phenyl] 2'-methyl-4'-(5-methyl-1,2,4-oxadiazol-3-yl)biphenyl-4- carboxamide (1; GR127935) as potent and selective 5-HT(1B/1D) antagonists were synthesized and evaluated pharmacologically. Their receptor binding profiles were comparable to that of 1. The 1,3,4-oxadiazole isomer 2 and the 4'-aminocarbonyl and 4'-

amidinyl analogues (9 and 10) of 1 had higher affinities at the rat 5-HT(1B) receptor (IC(50) = 0.93, 1. 3, and 0.5 nM, respectively) and calf 5-HT(1D) receptor (IC(50) = 37, 10, and 3 nM, respectively) than did 1 (1.6 and 52 nM for rat 5-HT(1B) and calf 5-HT(1D) receptors, respectively). In the functional in vitro testing of 5-HT(1B/1D) antagonistic properties, 2, 9, 10, 11b (O-demethylated derivative of 2), 13a (O-methylsulfonyl analogue of 2), and 16 (which differs from 2 with a sulfonamide linker) showed more pronounced effects in the K(+)-induced 5-HT release in the cortex of guinea pig than did 1 and 3 (SB224289). Compounds 2, 9, and 10 were equally potent as 1 in rabbit saphenous vein model (pA(2) > 9). A biochemical study of 2 with in vivo microdialysis in the rat brain showed that it is capable of augmenting citalopram (a selective serotonin reuptake inhibitor, SSRI) induced 5-HT release in rat ventral hippocampus, while preventing the decrease in acetylcholine release elicited by citalopram administration. The molecular structure of 2 was determined by single- crystal X-ray analysis. The log P and log D values of these compounds were calculated. This study contributes to the SAR study of N-piperazinylphenyl biphenylcarboxamides as selective and potent 5-HT(1B/1D) antagonists.

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FILE LAST UPDATED: 18 Sep 2007  (20070918/ED)

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L3          16 SEA SSS SAM L1 OR L2
L4             STR L1
L5             STR L***
L6          28 SEA SSS SAM L4 OR L5
L7         454 SEA SSS FUL L4 OR L5
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L10         9065 SEA ABB=ON  PLU=ON  L7
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L12        16134 SEA ABB=ON  PLU=ON  L7
L13          679 SEA ABB=ON  PLU=ON  L8 AND (METHOD OR PREP?)
L14         1181 SEA ABB=ON  PLU=ON  L9 AND (METHOD OR PREP?)
L15         1786 SEA ABB=ON  PLU=ON  L10 AND (METHOD OR PREP?)
L16          923 SEA ABB=ON  PLU=ON  L11 AND (METHOD OR PREP?)
     TOTAL FOR ALL FILES
L17         4569 SEA ABB=ON  PLU=ON  L12 AND (METHOD OR PREP?)
L18       868119 SEA ABB=ON  PLU=ON  CRYSTALL? OR PURIF?
L19       462956 SEA ABB=ON  PLU=ON  CRYSTALL? OR PURIF?
L20       316868 SEA ABB=ON  PLU=ON  CRYSTALL? OR PURIF?
L21      1768748 SEA ABB=ON  PLU=ON  CRYSTALL? OR PURIF?
     TOTAL FOR ALL FILES
L22      3416691 SEA ABB=ON  PLU=ON  CRYSTALL? OR PURIF?
L23            8 SEA ABB=ON  PLU=ON  L13 AND L18
L24           20 SEA ABB=ON  PLU=ON  L14 AND L19
L25           12 SEA ABB=ON  PLU=ON  L15 AND L20
L26           62 SEA ABB=ON  PLU=ON  L16 AND L21
     TOTAL FOR ALL FILES
L27          102 SEA ABB=ON  PLU=ON  L17 AND L22

     FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 18:16:39 ON 19 SEP 2007
L28            8 SEA ABB=ON  PLU=ON  L13 AND L18
L29           20 SEA ABB=ON  PLU=ON  L14 AND L19
L30           12 SEA ABB=ON  PLU=ON  L15 AND L20
     TOTAL FOR ALL FILES
L31           40 SEA ABB=ON  PLU=ON  L27
L32           33 DUP REM L31 (7 DUPLICATES REMOVED)
                 D 1-33 IBIB ABS

     FILE 'CAPLUS' ENTERED AT 18:17:07 ON 19 SEP 2007
L33           62 SEA ABB=ON  PLU=ON  L16 AND L21
L34           31 SEA ABB=ON  PLU=ON  L33 AND PD<DEC 2003
                 D 1-31 IBIB ABS HITSTR
L35          194 SEA ABB=ON  PLU=ON  MEI R?/AU
L36         2248 SEA ABB=ON  PLU=ON  GUO D?/AU
L37        35931 SEA ABB=ON  PLU=ON  WANG S?/AU
L38            1 SEA ABB=ON  PLU=ON  L35 AND L36 AND L37
                 D IBIB ABS HITSTR
L39            3 SEA ABB=ON  PLU=ON  (L35 OR L36 OR L37) AND L7
L40            2 SEA ABB=ON  PLU=ON  L39 NOT L38
                 D 1-2 IBIB ABS HITSTR

     FILE 'REGISTRY' ENTERED AT 18:21:10 ON 19 SEP 2007
                 E CITALOPRAM/CN 5
L41           21 SEA ABB=ON  PLU=ON  ?CITALOPRAM?/CNS

     FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 18:21:59 ON 19 SEP 2007
L42            4 SEA ABB=ON  PLU=ON  (L41 OR CITALOPRAM?)(L)CRYSTAL?
L43            7 SEA ABB=ON  PLU=ON  (L41 OR CITALOPRAM?)(L)CRYSTAL?
L44            4 SEA ABB=ON  PLU=ON  (L41 OR CITALOPRAM?)(L)CRYSTAL?
L45           38 SEA ABB=ON  PLU=ON  (L41 OR CITALOPRAM?)(L)CRYSTAL?
     TOTAL FOR ALL FILES
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L46          53 SEA ABB=ON  PLU=ON  (L41 OR CITALOPRAM?)(L) CRYSTAL?
L47           4 SEA ABB=ON  PLU=ON  L42 NOT (L38 OR L39 OR L28)
L48           7 SEA ABB=ON  PLU=ON  L43 NOT (L38 OR L39 OR L29)
L49           4 SEA ABB=ON  PLU=ON  L44 NOT (L38 OR L39 OR L30)

     FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 18:22:57 ON 19 SEP 2007
L50           4 SEA ABB=ON  PLU=ON  L42 NOT (L38 OR L39 OR L28)
L51           7 SEA ABB=ON  PLU=ON  L43 NOT (L38 OR L39 OR L29)
L52           4 SEA ABB=ON  PLU=ON  L44 NOT (L38 OR L39 OR L30)
     TOTAL FOR ALL FILES
L53          15 SEA ABB=ON  PLU=ON  L46 NOT (L38 OR L39 OR L31)
L54           7 DUP REM L53 (8 DUPLICATES REMOVED)
                D 1-7 IBIB ABS

     FILE 'CAPLUS' ENTERED AT 18:23:28 ON 19 SEP 2007

=> s 146 not l33
L55          10 L45 NOT L33

=> d 1-10 ibib abs

L55  ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:771986  CAPLUS  Full-text
TITLE:                    New process for the preparation of high pure
                          citalopram salts
INVENTOR(S):              Satyanarayana, Chava; Haribabu, Bodepudi;
                          Ramanjaneyulu, Gorantla Seeta; Jyothibasu, Abbineni;
                          Rao, Chunchu Venkata Ramana
PATENT ASSIGNEE(S):       Matrix Laboratories Ltd., India
SOURCE:                   Indian Pat. Appl.
                          CODEN: INXXBQ
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
     ---------------      ----   --------    -------------------    --------
     IN 2003CH00329        A     20070706    IN 2003-CH329          20030421
PRIORITY APPLN. INFO.:                       IN 2003-CH329          20030421
AB   The present invention claims the usage of excess cuprous cyanide to get the 5-
     bromo analogue levels to less than 0.3% in the crude citalopram, and rapid
     process for the isolation of pure citalopram salts in the absence of or with
     low levels «0.1 %) of the impurities by the judicious selection of solvents
     and the manipulation of pH without employing elaborate workup procedures
     including crystallization techniques or expensive film distillation.


L55  ANSWER 2 OF 10  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:681003  CAPLUS  Full-text
DOCUMENT NUMBER:          147:177535
TITLE:                    Synthesis and crystal structure of escitalpram oxalate
AUTHOR(S):                Song, Wei; Liu, Wenzheng; Zhao, Kang; Zhang, Guangming
CORPORATE SOURCE:         College of Pharmaceuticals and Biotechnology, Tianjin
                          University, Tianjin, 300073, Peop. Rep. China
SOURCE:                   Yaowu Fenxi Zazhi (2006), 26(3), 365-368
                          CODEN: YFZADL; ISSN: 0254-1793
PUBLISHER:                Yaowu Fenxi Zazhi Bianji Weiyuanhui
DOCUMENT TYPE:            Journal
LANGUAGE:                 Chinese
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AB Escitalpram oxalate was synthesized by the reaction of S- citalopram and oxalic acid in ethanol, and single crystal structure was determined by single-crystal X-ray diffraction method. The crystal belonged to the monoclinic system space group P2(1)/n, with cell parameters: a=8.031(3)Å, b=25.063(8)Å, c=11.122(4)Å, β=106.627(5)°, Z=4, V=2145.2(12)A3, Dc=1.283 g/cm3, u(MoKa)=0.097 mm-1, F(000)=872, the final R1=0.0629, and wR2=0.1566. X-ray anal. revealed that the C (1), C (2), C (3), C (4), C (5) and C (6) atoms formed a six-membered ring, which adopted the planar conformation; the C (8), C (9), C (10), C (11), C (13) and C (14) atoms formed a six-membered ring, which also adopted the planar conformation; and the C (7), C (8), C (14), C (15) and O (1) atoms formed a five-membered ring, which adopted the envelope conformation.

L55 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1301872 CAPLUS Full-text
DOCUMENT NUMBER: 144:80577
TITLE: Putative drug binding conformations of monoamine transporters
AUTHOR(S): Ravna, Aina Westrheim; Sylte, Ingebrigt; Kristiansen, Kurt; Dahl, Svein G.
CORPORATE SOURCE: Department of Pharmacology, Institute of Medical Biology, University of Tromso, Tromso, N-9037, Norway
SOURCE: Bioorganic & Medicinal Chemistry (2006), 14(3), 666-675
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Structural information about monoamine transporters and their interactions with psychotropic drugs is important for understanding their mol. mechanisms of action and for drug development. The crystal structure of a Major Facilitator Superfamily (MFS) transporter, the lactose permease symporter (lac permease), has provided insight into the three-dimensional structure and mechanisms of secondary transporters. Based on the hypothesis that the 12 transmembrane α-helix (TMH) secondary transporters belong to a common folding class, the lac permease structure was used for mol. modeling of the serotonin transporter (SERT), the dopamine transporter (DAT), and the noradrenaline transporter (NET). The mol. modeling methods used included amino acid sequence alignment, homol. modeling, and mol. mech. energy calcns. The lac permease crystal structure has an inward-facing conformation, and construction of outward-facing SERT, DAT, and NET conformations allowing ligand binding was the most challenging step of the modeling procedure. The psychomotor stimulants cocaine and S-amphetamine, and the selective serotonin reuptake inhibitor (SSRI) S-citalopram, were docked into putative binding sites on the transporters to examine their mol. binding mechanisms. In the inward-facing conformation of SERT the translocation pore was closed towards the extracellular side by hydrophobic interactions between the conserved amino acids Phe105, Pro106, Phe117, and Ala372. An unconserved amino acid, Asp499 in TMH10 in NET, may contribute to the low affinity of S-citalopram to NET.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:100600 CAPLUS Full-text
DOCUMENT NUMBER: 143:16772
TITLE: 5-Bromo-3H-isobenzofuran-1-one (5-bromophthalide)
AUTHOR(S): Yathirajan, Hemmige S.; Nagaraj, Basavegowda; Gaonkar, Santhosh L.; Narasegowda, Rajenahally S.; Nagaraja, Padmarajaiah; Bolte, Michael

CORPORATE SOURCE: Department of Studies in Chemistry, University of Mysore, Mysore, 570 006, India
SOURCE: Acta Crystallographica, Section E: Structure Reports Online (2005), E61(2), o345-o346
CODEN: ACSEBH; ISSN: 1600-5368
URL: http://journals.iucr.org/e/graphics/htmlborder.gif
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The title compound, C8H5BrO2, serves as a starting material for the synthesis of citalopram. Crystallog. data are given. It crystallizes with two almost identical mols. in the asym. unit.
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:100599 CAPLUS Full-text
DOCUMENT NUMBER: 143:16771
TITLE: 5-Amino-3H-isobenzofuran-1-one (5-aminophthalide)
AUTHOR(S): Yathirajan, Hemmige S.; Nagaraj, Basavegowda; Gaonkar, Santhosh L.; Narasegowda, Rajenahally S.; Prabhuswamy, Basappa; Bolte, Michael
CORPORATE SOURCE: Department of Studies in Chemistry, University of Mysore, Mysore, 570 006, India
SOURCE: Acta Crystallographica, Section E: Structure Reports Online (2005), E61(2), o343-o344
CODEN: ACSEBH; ISSN: 1600-5368
URL: http://journals.iucr.org/e/graphics/htmlborder.gif
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The title compound, C8H7NO2, serves as an intermediate for the synthesis of citalopram. Crystallog. data are given. The packing of the planar mols. is stabilized by N-H···O and N-H···N H bonds.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:589419 CAPLUS Full-text
DOCUMENT NUMBER: 141:128865
TITLE: Carbostyril derivatives and serotonin reuptake inhibitors for treatment of mood disorders
INVENTOR(S): Kikuchi, Tetsuro; Iwamoto, Taro; Hirose, Tsuyoshi
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004060374	A1	20040722	WO 2003-JP16724	20031225

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,

PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2511619	A1	20040722	CA 2003-2511619	20031225
AU 2003295235	A1	20040729	AU 2003-295235	20031225
EP 1575590	A1	20050921	EP 2003-786308	20031225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003017771	A	20051122	BR 2003-17771	20031225
CN 1726039	A	20060125	CN 2003-80106103	20031225
EP 1723957	A2	20061122	EP 2006-17539	20031225
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR, LT, LV				
CN 1989968	A	20070704	CN 2007-10001620	20031225
JP 2004217650	A	20040805	JP 2003-433429	20031226
NO 2005002359	A	20050718	NO 2005-2359	20050512
ZA 2005003873	A	20060830	ZA 2005-3873	20050513
MX 2005PA06857	A	20050818	MX 2005-PA6857	20050622
IN 2005KN01229	A	20060630	IN 2005-KN1229	20050624
US 2006154938	A1	20060713	US 2005-540577	20051216
PRIORITY APPLN. INFO.:			JP 2002-379003 A	20021227
			US 2003-470481P P	20030514
			CN 2003-80106103 A3	20031225
			EP 2003-786308 A3	20031225
			WO 2003-JP16724 W	20031225

AB The pharmaceutical composition of the present invention comprises (1) a carbostyril derivative and (2) a serotonin reuptake inhibitor in a pharmaceutically acceptable carrier. The carbostyril derivative may be aripiprazole or a metabolite thereof, which is a dopamine-serotonin system stabilizer. The serotonin reuptake inhibitor may be fluoxetine, duloxetine, venlafaxine, milnacipran, citalopram, fluvoxamine, paroxetine, sertraline or escitalopram. The pharmaceutical composition of the present invention is useful for treating patients with mood disorders, particularly depression or major depressive disorder. For example, a tablet formulation contained aripiprazole anhydride crystals B 5 mg, venlafaxine 75 mg, starch 131 mg, magnesium stearate 4 mg, and lactose 60 mg.

L55 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:696079 CAPLUS Full-text
DOCUMENT NUMBER: 139:219273
TITLE: Preparation of citalopram salts
INVENTOR(S): Hamied, Yusuf Khwaja; Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra
PATENT ASSIGNEE(S): Cipla Limited, India
SOURCE: Brit. UK Pat. Appl., 7 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2385848	A	20030903	GB 2002-4683	20020227
WO 2003072563	A1	20030904	WO 2003-GB816	20030226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003208448	A1	20030909	AU 2003-208448	20030226
EP 1478637	A1	20041124	EP 2003-706736	20030226
EP 1478637	B1	20050810		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008063	A	20041228	BR 2003-8063	20030226
IN 2004MN00543	A	20050520	IN 2004-MN543	20040930
PRIORITY APPLN. INFO.:			GB 2002-4683 A	20020227
			WO 2003-GB816 W	20030226

AB Amorphous pharmaceutically acceptable salts of citalopram are made by spray drying, lyophilization or evaporation of solns. and may be incorporated into pharmaceutical compns. Citalopram hydrobromide 20 g, was dissolved in 200 mL methanol and spray dried with an inlet temperature of 110 °C, outlet temperature of 67 °C and feed rate of 5 mL/min to obtain amorphous citalopram hydrobromide.

L55 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:312345 CAPLUS Full-text

DOCUMENT NUMBER: 139:52845

TITLE: Interaction of cis-(6-Benzhydrylpiperidin-3-yl)benzylamine Analogues with Monoamine Transporters: Structure-Activity Relationship Study of Structurally Constrained 3,6-Disubstituted Piperidine Analogues of (2,2-Diphenylethyl)-[1-(4-fluorobenzyl)piperidin-4-ylmethyl]amine

AUTHOR(S): Kolhatkar, Rohit B.; Ghorai, Sujit K.; George, Clifford; Reith, Maarten E. A.; Dutta, Aloke K.

CORPORATE SOURCE: Department of Pharmaceutical Sciences, Wayne State University, Detroit, MI, 48202, USA

SOURCE: Journal of Medicinal Chemistry (2003), 46(11), 2205-2215
CODEN: JMCMAR; ISSN: 0022-2623

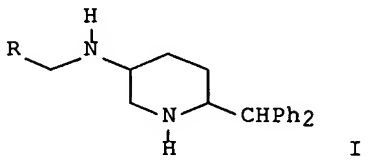
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:52845

GI



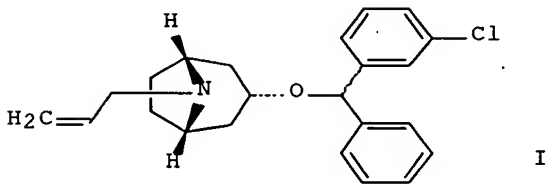
I

AB To explore structure-activity relationships (SAR) of a novel conformationally constrained lead cis-3,6-disubstituted piperidine derivative derived from

(2,2-diphenylethyl)-[1-(4-fluorobenzyl)piperidine-4- ylmethyl]amine, a series of racemic and optically active substituted Ph and heterocyclic derivs. I (R = Ph, 4-NCC6H4, 4-FC6H4CH2, 2-thienyl, 3-indolyl, etc.) was synthesized by derivatizing the exocyclic N-atom at the 3-position of the lead. All novel compds. were tested for their affinity at the dopamine transporter (DAT), serotonin transporter (SERT), and norepinephrine transporter (NET) in the brain by measuring their potency in competing for the binding of [3H]WIN 35 428, [3H] citalopram, and [3H]nisoxetine, resp. Selected compds. were also evaluated for their activity in inhibiting the uptake of [3H]DA. The SAR results demonstrated that the nature of substitutions on the Ph ring is important in activity at the DAT with the presence of an electron-withdrawing group having the maximum effect on potency. Replacement of the Ph ring in the benzyl group by heterocyclic moieties resulted in the development of compds. with moderate activity for the DAT. Two most potent racemic compds., I (R = 4-FC6H4, 4-NCC6H4), were separated by a diastereoisomeric separation procedure, and differential affinities were observed for the enantiomers. Absolute configuration of the enantiomers was obtained unambiguously by X-ray crystal structural study. One of the enantiomers, S,S-(-)-I (R = 4-NCC6H4), exhibited the highest potency for the DAT (IC50 = 11.3 nM) among all the compds. tested and was as potent as GBR 12909 (1-[2-[bis(4-fluorophenyl)methoxy]ethyl]-4-(3- phenylpropyl)piperazine). However, S,S-(-)-I (R = 4-NCC6H4) was more selective than GBR 12909 in binding to the DAT compared with binding to the SERT and NET. The present results establish the newly developed 3,6-disubstituted piperidine derivs. as a novel template for high-affinity inhibitors of DAT.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:28291 CAPLUS Full-text
DOCUMENT NUMBER: 134:222890
TITLE: Structure-Activity Relationships at Monoamine Transporters and Muscarinic Receptors for N-Substituted-3α-(3'-chloro-, 4'-chloro-, and 4',4''-dichloro-substituted-diphenyl)methoxytropanes
AUTHOR(S): Newman, Amy Hauck; Robarge, Michael J.; Howard, Ileana M.; Wittkopp, Sharine L.; George, Clifford; Kopajtic, Theresa; Izenwasser, Sari; Katz, Jonathan L.
CORPORATE SOURCE: Medicinal Chemistry and Psychobiology Sections, National Institute on Drug Abuse-Intramural Research Program, Baltimore, MD, 21224, USA
SOURCE: Journal of Medicinal Chemistry (2001), 44(4), 633-640
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:222890
GI



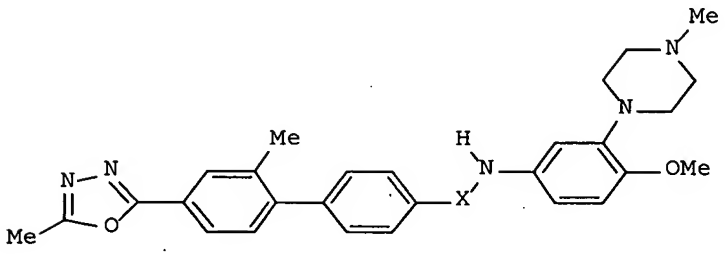
I

AB The design, synthesis, and evaluation of 3α-(diphenylmethoxy)tropane (benztropine) analogs, e.g. I, have provided potent and selective probes for the dopamine transporter. Structure-activity relationships (SARs) have been developed that contrast with those described for cocaine, despite significant structural similarity. Furthermore, behavioral evaluation of many of the benztropine analogs in animal models of cocaine abuse has suggested that these two classes of tropane-based dopamine uptake inhibitors have distinct pharmacol. profiles. In general, the benztropine analogs do not demonstrate efficacious locomotor stimulation in mice, do not fully substitute for a cocaine discriminative stimulus, and are not appreciably self-administered in rhesus monkeys. These compds. are generally more potent than cocaine as dopamine uptake inhibitors in vitro, although their actions in vivo are not consistent with this action. These observations suggest that differing binding profiles at the serotonin and norepinephrine transporters as well as at muscarinic receptors might have significant impact on the pharmacol. actions of these compds. In addition, by varying the structures of the parent compds. and thereby modifying their phys. properties, pharmacokinetics as well as pharmacodynamics will be directly affected. Therefore, in an attempt to systematically evaluate the impact of chemical modification on these actions, a series of N-substituted (H, CH3, allyl, benzyl, propylphenyl, and butylphenyl) analogs of 3'-chloro-, 4'-chloro-, and 4,4''-dichloro-3α-(diphenylmethoxy)tropanes were synthesized. These compds. were evaluated for displacement, in rat tissue, of [3H]WIN 35,428 from the dopamine transporter, [3H]citalopram from the serotonin transporter, [3H]nisoxetine from the norepinephrine transporter, and [3H]pirenzepine from muscarinic m1 receptors. SARs were developed and compared to a series of N-substituted-3α-(bis-4'-fluorophenyl)methoxytropanes. The present SARs followed previously reported studies with the single exception of the N-butylphenyl substituent, which did not provide the high affinity binding in any of these three sets of analogs, as it did in the 4',4''-difluoro series. X-ray crystallog. analyses of the three parent ligands were compared to that of 3α-(bis-4'-fluorophenyl)methoxytropane which provided supportive evidence toward the proposal that the combination of steric bulk in both the 3-position and the N-substituent, in this class of compds., is not optimal for binding at the dopamine transporter. These studies provide binding profile data that can now be used to correlate with future behavioral analyses of these compds. and may provide insight into the kind of binding profile that might be targeted as a potential treatment for cocaine abuse.

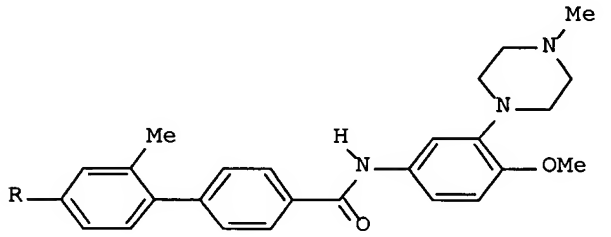
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:45848 CAPLUS Full-text
DOCUMENT NUMBER: 132:207827
TITLE: New selective and potent 5-HT1B/1D antagonists: chemistry and pharmacological evaluation of N-piperazinylphenyl biphenylcarboxamides and biphenylsulfonamides
AUTHOR(S): Liao, Yi; Boettcher, Henning; Harting, Juergen; Greiner, Hartmut; Van Amsterdam, Christoph; Cremers, Thomas; Sundell, Staffan; Maerz, Joachim; Rautenberg, Wilfried; Wikstroem, Haakan
CORPORATE SOURCE: Department of Medicinal Chemistry Center for Pharmacy, University of Groningen, Groningen, NL-9713 AV, Neth.
SOURCE: Journal of Medicinal Chemistry (2000), 43(3), 517-525
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



II



III

AB A series of new analogs of N-[4-methoxy-3-(4-methylpiperazin-1-yl)phenyl] 2'-methyl-4'-(5-methyl-1,2,4-oxadiazol-3-yl)biphenyl-4-carboxamide (I; GR127935) as potent and selective 5-HT1B/1D antagonists were synthesized and evaluated pharmacol. Their receptor binding profiles were comparable to that of I. The 1,3,4-oxadiazole isomer II (X = C:O) and the 4'-aminocarbonyl and 4'-amidinyl analogs III [R = CONH2, C(NH2):NH] had higher affinities at the rat 5-HT1B receptor (IC50 = 0.93, 1.3, and 0.5 nM, resp.) and calf 5-HT1D receptor (IC50 = 37, 10, and 3 nM, resp.) than did I (1.6 and 52 nM for rat 5-HT1B and calf 5-HT1D receptors, resp.). In the functional in vitro testing of 5-HT1B/1D antagonistic properties, II, III, the O-demethylated derivative of II, the O-methylsulfonyl analog of II, and sulfonamide II (X = SO2) showed more pronounced effects in the K+-induced 5-HT release in the cortex of guinea pig than did I and SB224289. Compds. II and III were equally potent as I in rabbit saphenous vein model (pA2 > 9). A biochem. study of II with in vivo microdialysis in the rat brain showed that it is capable of augmenting citalopram (a selective serotonin reuptake inhibitor, SSRI) induced 5-HT release in rat ventral hippocampus, while preventing the decrease in acetylcholine release elicited by citalopram administration. The mol. structure of II was determined by single- crystal X-ray anal. The log P and log D values of these compds. were calculated This study contributes to the SAR study of N-piperazinylphenyl biphenylcarboxamides as selective and potent 5-HT1B/1D antagonists.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> dis his nofile

(FILE 'HOME' ENTERED AT 18:10:43 ON 19 SEP 2007)

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     FILE 'REGISTRY' ENTERED AT 18:10:48 ON 19 SEP 2007
L1                STR
L2                STR L1
L3             16 SEA SSS SAM L1 OR L2
L4                STR L1
L5                STR L***
L6             28 SEA SSS SAM L4 OR L5
L7            454 SEA SSS FUL L4 OR L5
                  D L7 QUE STAT

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L9          2783 SEA ABB=ON  PLU=ON  L7
L10         9065 SEA ABB=ON  PLU=ON  L7
L11         2372 SEA ABB=ON  PLU=ON  L7
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L12        16134 SEA ABB=ON  PLU=ON  L7
L13          679 SEA ABB=ON  PLU=ON  L8 AND (METHOD OR PREP?)
L14         1181 SEA ABB=ON  PLU=ON  L9 AND (METHOD OR PREP?)
L15         1786 SEA ABB=ON  PLU=ON  L10 AND (METHOD OR PREP?)
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L18       868119 SEA ABB=ON  PLU=ON  CRYSTALL? OR PURIF?
L19       462956 SEA ABB=ON  PLU=ON  CRYSTALL? OR PURIF?
L20       316868 SEA ABB=ON  PLU=ON  CRYSTALL? OR PURIF?
L21      1768748 SEA ABB=ON  PLU=ON  CRYSTALL? OR PURIF?
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L23            8 SEA ABB=ON  PLU=ON  L13 AND L18
L24           20 SEA ABB=ON  PLU=ON  L14 AND L19
L25           12 SEA ABB=ON  PLU=ON  L15 AND L20
L26           62 SEA ABB=ON  PLU=ON  L16 AND L21
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L27          102 SEA ABB=ON  PLU=ON  L17 AND L22

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L30           12 SEA ABB=ON  PLU=ON  L15 AND L20
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L31           40 SEA ABB=ON  PLU=ON  L27
L32           33 DUP REM L31 (7 DUPLICATES REMOVED)
                  D 1-33 IBIB ABS

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L34           31 SEA ABB=ON  PLU=ON  L33 AND PD<DEC 2003
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L35          194 SEA ABB=ON  PLU=ON  MEI R?/AU
L36         2248 SEA ABB=ON  PLU=ON  GUO D?/AU
L37        35931 SEA ABB=ON  PLU=ON  WANG S?/AU
L38            1 SEA ABB=ON  PLU=ON  L35 AND L36 AND L37
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L39            3 SEA ABB=ON  PLU=ON  (L35 OR L36 OR L37) AND L7
L40            2 SEA ABB=ON  PLU=ON  L39 NOT L38
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     FILE 'REGISTRY' ENTERED AT 18:21:10 ON 19 SEP 2007
                  E CITALOPRAM/CN 5
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L41          21 SEA ABB=ON  PLU=ON  ?CITALOPRAM?/CNS

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L43           7 SEA ABB=ON  PLU=ON  (L41 OR CITALOPRAM?)(L)CRYSTAL?
L44           4 SEA ABB=ON  PLU=ON  (L41 OR CITALOPRAM?)(L)CRYSTAL?
L45          38 SEA ABB=ON  PLU=ON  (L41 OR CITALOPRAM?)(L)CRYSTAL?
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L46          53 SEA ABB=ON  PLU=ON  (L41 OR CITALOPRAM?)(L) CRYSTAL?
L47           4 SEA ABB=ON  PLU=ON  L42 NOT (L38 OR L39 OR L28)
L48           7 SEA ABB=ON  PLU=ON  L43 NOT (L38 OR L39 OR L29)
L49           4 SEA ABB=ON  PLU=ON  L44 NOT (L38 OR L39 OR L30)

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L52           4 SEA ABB=ON  PLU=ON  L44 NOT (L38 OR L39 OR L30)
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L53          15 SEA ABB=ON  PLU=ON  L46 NOT (L38 OR L39 OR L31)
L54           7 DUP REM L53 (8 DUPLICATES REMOVED)
                D 1-7 IBIB ABS

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                D 1-10 IBIB ABS

=> d 17 que stat
L4                STR
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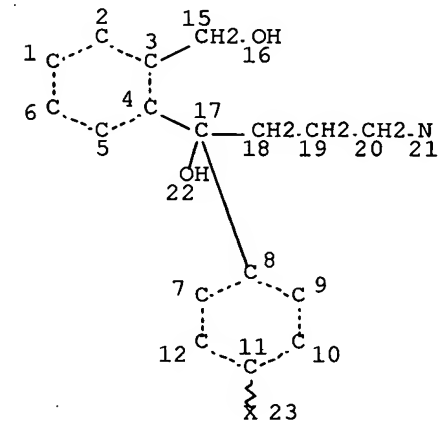


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NUMBER OF NODES IS  21

STEREO ATTRIBUTES: NONE
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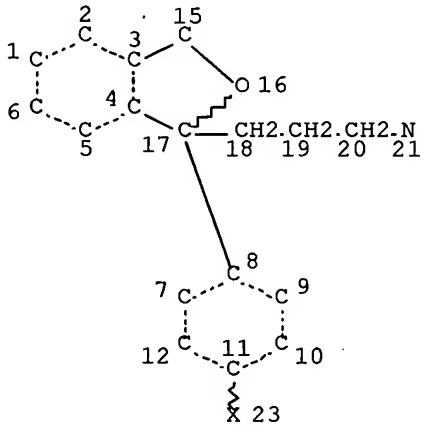

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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
L7 454 SEA FILE=REGISTRY SSS FUL L4 OR L5

100.0% PROCESSED 615 ITERATIONS 454 ANSWERS
SEARCH TIME: 00.00.01

=> log y

STN INTERNATIONAL LOGOFF AT 18:25:23 ON 19 SEP 2007